FIG. 1A

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- GTTGATTGAT CAACTAACTA ACCAACAGCG C TCATTGCTGA GTTGTTATTT AAGCTTGCCC AGTAACGACT CAACAATAAA TTCGAACGGG AGCTITGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG TCGAAACCTC TAATAGCAGT GACGTIACGA AGCGTTATAC CGCGTTTTAC TIGGATAAGG AAATACAGAC ATGAAAAATC AACCIATITCC TITATGICTG TACTITITAG ATTATCGTCA AGCTTTGGAG CTTGACACAC GCGTCCATCT CTTAAGTIGA AGAGGTATGA CGCAGGTAGA GAACTGTGTG 101
- AACTICGIAG GAGCAGICAI CTCGTCAGTA TTGAAGCATC GOGCECTGTA CAAGGTAAAG CCCGATGCCA GCATTCCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA ' CCCGCGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT , 201
- TGTTTTTATT TTTTAATGTA TTTGTAACTA GTACGCAAGT ACAAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA GCTGTCATAA AGTTGTCACG GCCGAGACTT ATAGTCGCTT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA CITITCAACA G PARAGITARI TTTTCAATTA
- TCTATTGCTA CAAACGCGTA CGCTGATATC CAAGCAAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG F V F S I A T N A Y A D I GITCGITITI TTGCATCTAT C S Ø GAAGAATATC GCATTTCTTC
 CTTCTTATAG CGTAAAGAAG AFLL 'STII Signal Sequence TIR-1 z z GAATTATGAA C × AGGGTATCTA (TCACGTAAAA AGTGCATTTT 401
- CTGAACTGGT GACTTGACCA 3 2 CAAGAGCTAT GTTCTCGATA CAGCGCTGTA GTCGCGACAT Ω ACGTCTCGGT (TGCAGAGCCA GTGGTAGTGG) CACCATCACC CGCTATCCCA GCGATAGGGT Ω CTCCCTGTCC C ഗ J w AGTCCCCGAG TCAGGGGCTC တ CAGATGACCC A E o 201 56
- CAAGACCCTG AGACCTAGGC (O TTCTCGCTTC œ AAGGAGTCCC TTCCTCAGGG > ပ TCAGAGCGAC AGTCTCGCTG 4 GATACGATGA CTATGCTACT TACTGATTTA CGAGGCTTTC ATGACTAAAT A P K V L I Y GCTCCGAAAG TGGTCCTTTT P G K ACCAGGAAAA TAGTIGICTI o 501 9
- TGTCCCATGG 0 GGACATTTGG CCTGTAAACC CTCAGAGGTA GAGTCTCCAT . S TCAGCACGGA × TAATGACAGA ATTACTGTCT ပ **≻** TTCGCAACTT AAGCGTTGAA æ GCCAGAAGAC CGGTCTTCTG Ω ω Δ, GCAGTCTGCA (0 u ဟ CTGACCATCA GACTGGTAGT ഗ LII GGATTACACT CCTAATGTGA χ Ω 107 93
- CACACGGACG ... ACGAAGACAA TGCTTCTGTT TTAGACCTTG AATCTGGAAC CTCGTCAACT : GAGCAGTTGA GCCATCTGAT CGGTAGACTA S TCATCTTCCC AGTAGAAGGG (ı, GGTAGACAGA A P S V F CCATCTGTCT AGTIIGCIIG ACACCGACGI K R I V A A TGTGGCTGCA TCAAACGAAC TTCCACCTCT K V E I AAGGTGGAGA
- GTCACAGAGC CAGTGTCTCG CCAGGAGAGT GGTCCTCTCA ш 0 GGGTAACTC GGCCATTGAG G z ပ GCCCTCCAAT CGGGAGGTTA . O CCACCTATTG GGTGGATAAC z Ω > TACAGTGGAA ATGTCACCTT × 3 0 GAGGCCAAAG CICCGGIIIC × CTATCCCAGA GATAGGGTCT Ω, >-ACTIATIGAA TGAATAACTT z 901
- CCCGGACTCG AGTGGGTAGT CGGACGCTTC U CANAGICTAC GITICAGAIG ACGAGAAACA TGCTCTTTGT ω TTTCGTCTGA AAAGCAGACT Ω GACGCTGAGC A CTGCGACTCG 1 T L S A CGTCGTGGGA S ATGTCGGAGT Y S L S CCTGTCGTGG
- AGCTCGGTAC CCGGGGATCT AGGCCTAACG TCGAGCCATG GGCCCCTAGA TCCGGATTGC GAGTGTTAAT TAAATCCTCT ACGCCGGACG CATCGTGGCG CTCACAATTA ATTTAGGAGA TGCGGCCTGC GTAGCACCGC GITGICCCCI z GTTTCTCGAA TCGCCCGTCA AGCGGGCAGT s

AGGTGCATAA TCCACGTATT V H N

GACGGCGTGG A CTGCCGCACC I D G V E

2401 TCTCCCGGAC CCCTGAGGTC ACATGCGTGG TGGTGGACGT GAGCCACGAA GACCCTGAGG TCAAGTTCAA CTGGTACGTG AGAGGGCCTG GGGACTCCAG TGTACGCACC ACCACCTGCA CTCGGTGCTT CTGGGACTCC AGTTCAAGTT GACCATGCAC 277 S R T P E V T C v v v D v S H E D P E v K F N W Y V

ACCCTCATGA TGGGAGTACT

TCCCCCCAAA A AGGGGGGTTT 1

GTCTTCCTCT 1 CAGAAGGAGA A V F L F

GGGACCGTCA Ω, v

C CCAGCACCTG AACTCCTGGG G G GGTCGTGGAC TTGAGGACCC CI P A P E L L G (

TGTGACAJAA CTCACACATG CCCACCGTGC ACACTGITIT GAGTGTGTAC GGGTGGCACG

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GAGCCAACGG CGGCCCGCAA AAAATAACAA CGGCTGCGCG TAGAGCTTAC TTGACACACG CGTCCATCTT CGAAACLICI AAIAGCAGIG ACGIACACAA	CGCAATATGG CGCAAAATGA CCAACAGGGG TTGATTGATC AGGTAGAGGG GGCGCTGTAC GAGGTAAAGC CCGATGCCAG CATTCCTGAC GACGATACGG GCGTTATACC GCGTTTTACT GGTTGTCGCC AACTAACTAG TCCATCTCCC CCGCGACATG CTCCATTTCG GGCTACGGTC GTAAGGACTG CTGCTATGCC	AAAGITAATC TTTTCAACAG CTGTCATAAA GTTGTCACGG CCGAGACTTA TTTCAATTAG AAAAGTTGTC GACAGTATTT CAACAGTGCC GGCTCTGAAT	TAGTCGCTIT GITITIAITI ITIAAIGIAI ITGIAACIAG TACGCAAGIT CACGTAAAAA GGGIAICTAG AATTAIGAAG AAGAATAICG CATTICTICT ATCAGCGAAA CAAAAAIAAA AAAITACAIA AACATIGAIC AIGCGTICAA GIGCAITITI CCCAIAGAIC TIAATACTIC ITCTIAIAGG GIAAAGAAGA A K K N I A F L L M K K N I A F L L SIGIA (SIGIA) SEQUENÇE TIR-1	IGCAICTAIG TICGTTITIT CTATIGCTAC AAACGCGTAC GCTGAGGTIC AGCTGGTGGA GTCTGGCGGT GGCCTGGTGC AGCCAGGGG CTCACTCCGT ACGTAGATAC AAGCAAAAA GATAACGAIG TTTGCGCATG CGACTCCAAG TCGACCACT CAGACCGCCA CCGGACCACG TCGGTCCCC GAGTGAGGCA A S M F V F S I A T N A Y A E V Q L V E S G G L V Q P G G S L R	1701 TIGICCIGIG CAGCTICIGG CTICAATATT AAGGAGTACT ACAIGCACIG GGICCGICAG GCCCCGGGIA AGGGCCIGGA AIGGGITGGA TIGATIGAIC AACAGGACAC GICGAAGACC GAAGTIATAA TICCICAIGA IGIACGIGAC CCAGGCACT CGGGGCCCAI TCCCGGACCT TACCCAACCT AACTAAACTAG 43 L S C A A S G F N I K E Y Y M H W V R Q A P G K G L E W V G L I D P	1801 CAGAGCAAGG CAACACGATC TATGACCCGA AGTTCCAGGA CCGTGCCACT ATAAGCGCTG ACAATTCCAA AAACACGGA TACCTGCAGA TGAACAGCCT GTCTCGTTCC GTTGTGCTAG ATACTGGGCT TCAAGGTCCT GGCACGGTGA TATTCGCGAC TGTTAAGGTT TTTGTGTGT ATGGACGTCT ACTTGTGGA 77 E Q G N T I Y D P K F Q D R A T I S A D N S K N T A Y L Q M N S L	1901 GCGTGCTGAG GACACTGCCG TCTATTATTG TGCTCGAGAC ACGGCCGCTT ACTTCGACTA CTGGGGTCAA GGAACCCTGG TCACCGTCTC CTCGGCCTCC CGCACGACTC CTGTGACGGC AGATAATAAC ACGAGCTCTG TGCCGCGAA TGAAGCTGAT GACCCCAGTT CCTTGGGACC AGTGGCAGA GAGCCGGAGG 110 R A E D T A V Y Y C A R D T A A Y F D Y W G O G T L V T V S S A S	2001 ACCAAGGGCC CATCGGTCTT CCCCCTGGCA CCTCCTCCA AGAGCACCTC TGGGGGCACA GCGGCCCTGG GCTGCCTGGT CAAGGACTAC TTCCCCGAAC TGGTTCCCGG GTAGCCAGAA GGGGGACCGT GGGAGGAGGT TCTCGTGGAG ACCCCCGTGT CGCCGGGACC CGACGGACCA GTTCCTGATG AAGGGGCTTG 143 T K G P S V F P L A P S S K S T S G G T A A L G C L V K D Y F P E P	2101 CGGTGACGGT GTCGTGGAAC TCAGGCGCCC TGACCAGCGG CGTGCACCC TTCCCGGCTG TCCTACAGTC CTCAGGACTC TACTCCCTCA GCAGCGTGGT GCCACTGCCA CAGCACCTTG AGTCCGCGGG ACTGGTCGC CCACGTGTGG AAGGGCCGAC AGGATGTCAG GAGTCCTGAG ATGAGGGAGT CGTCGCACCA 177 V T V S W N S G A L T S G V H T F P A V L Q S S G L Y S L S S V V	2201 GACTGIGCCC TCIAGCAGCT IGGGCACCCA GACCTACATC IGCAACGTGA ATCACAAGCC CAGCAACACC AAGGIGGACA AGAAAGITGA GCCCAAAICI CIGACACGGG AGAICGIGGA ACCCGIGGGI CIGGAIGIAG ACGIIGCACI IAGIGIICGG GICGIIGIGG IICCACCIGI ICITICAACI CGGGIIIAGA 210 I V P S S S L G I Q I Y I C N V N H K P S N T K V D K K V E P K S	ACTACTOR CACCAGOOCA ANACOCATOR TO THE TOTAL TOTA
TTGACACAC	GGCGCTGTA CCGCGACAT	AAAGTTAAT TTTCAATTA	CACGTAAAA GTGCATTTT	AGCTGGTGGA TCGACCACCT L V E issue Facto	GGTCCGTCA CCAGGCAGT V R Q	ATAAGCGC TATTCGCG/ I S A	ACTTCGACTA TGAGCTGAT F D Y	TGGGGGCAC ACCCCCGTG	TTCCCGCTG AAGGGCCGAC F P A V	ATCACAAG TAGTGTTC H K	
TAGAGCTTAC	AGGTAGAGGG TCCATCTCCC	TCGTCAGTAA	tacgcaagtt atgcgttcaa	CCTGAGGTTC CGACTCCAAG A E V O	ACATGCACTG TGTACGTGAC	CCGTGCCACT GGCACGGTGA R A T	ACGGCCGCTT TGCCGGCGAA T A A Y	AGAGCACCTC TCTCGTGGAG S T S	CGTGCACACC GCACGTGTGG V H T	TGCAACGTGA ACGTTGCACT C 'N V N	
COGCIOCOCO TAGAGCITAC ITGACAĈACO COICCAICII CGAAACCICI AAIAGCAGIG ALGIIALGAA	TTGATTGATC AACTAACTAG	TGAAGCATCC ACTTCGTAGG	TTGTAACTAG AACATTGATC	AAACGCGTAC TTTGCGCATG N A Y	CTTCAATATT AAGGAGTACT ACATGCACTG GAAGTTATAA TTCCTCATGA TGTACGTGAC F N I K E Y Y M H W	AGTTCCAGGA TCAAGGTCCT F Q D	TGCTCGAGAC ACGAGCTCTG A R D	CCCTCCTCCA GGGAGGAGGT P S S K	TGACCAGCGG ACTGGTCGCC T S G	GACCTACATC CTGGATGTAG T Y I	
AAAATAACAA	CCAACAGCGG GGTTGTCGCC	AAGAAGTTAT TTCTTCAATA	tttaatgtat Aaattacata	CTATTGCTAC GATAACGATG I A T	CTTCAATATT GAAGTTATAA F N I	TATGACCCGA ATACTGGGCT Y D P K	TCTATTATTG AGATAATAAC Y Y C	CCCCCTGGCA GGGGGACCGT P L A	TCAGGCGCCC AGTCCGCGGG S G A L	TGGGCACCCA ACCCGTGGGT G T Q	
CGGCCGCAA	CGCAAAATGA GCGTTTTACT	CGAITACGTA AAGAAGTTAT TGAAGCATCC TCGTCAGTAA AAAGTTAAATC GCTAATGCAT TTCTTCAATA ACTTCGTAGG AGCAGTCATT TTTCAATTAG	GTITITATIT TITAATGTAT TIGTAACTAG TACGCAAGTT CACGTAAAAA CAAAAATAAA AAATTACATA AACATTGATC ATGCGTTCAA GIGCATTITT	TTCGTTTTTT AAGCAAAAA F V F S	TIGICCTGIG CAGCTICTGG AACAGGACAC GTCGAAGACC L S C A A S G	CAACACGATC GTTGTGCTAG N T I	GACACTGCCG TCTATTATTG TGCTCGAGAC ACGGCCGCTT ACTTCGACTA CTGTGACGGC AGATAATAAC ACGAGCTCTG TGCCGGCGAA TGAAGCTGAT D T A V Y Y C A R D T A A Y F D Y	ACCAAGGGCC CATCGGTCTT CCCCCTGGCA CCTCCTCCA AGAGCACCTC TGGGGGCACA TGGTTCCCGG GTAGCCAGAA GGGGGACGT GGBGGAGGAGT TCTCGTGGAG ACCCCGTGT T K G P S V F P L A P S S K S T S G G T	CGGTGACGGT GTCGTGGAAC GCCACTGCCA CAGCACCTTG V T V S W N	TCTAGCAGCT AGATCGTCGA S S S L	
1201 CTCGGTTGCC GCCGGGGII IIIIAIIGII GAGCCAACGG CGGCCCGCAA AAAATAACAA		AGCTGCTGCG TCGACGACGC		TGCATCTATG ACGTAGATAC A S M	TTGTCCTGTG AACAGGACAC L S C A	CAGAGCAAGG GTCTCGTTCC E Q G	GCGTGCTGAG CGCACGACTC R A E	ACCAAGGGCC TGGTTCCCGG T K G P	CGGTGACGGT GCCACTGCCA V T V	GACTGTGCCC CTGACACGGG T V P	
1201	1301	1401	1501	1601	1701	1801	1901	2001	2101	2201	

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A D TG	ဂ် ဂိ	4 5 0	AG TC	ပ္ပုပ္ပ	34G 3TC	g ပို့	TT AA
GGAGT CCTCA E Y	CTGCC GACGG	ATGGG TACCG	60.00 00.10 0.0	GACGG	ATCAC	GGCTT	TGCAU
gar TTS	ACC 169	400 400 400	CAC	760 ACG	TT 44	ATA TAT	ACT
74769 7780	rgtag ACATG Y	SGAGA SCTCT E S	AGCAG FCGTC	VAGCA LTCGI	SGTAG	TAGGC	TGCGT
2501 IGCCAAGACA AAGCCGCGGG AGGAGCAGIA CAACAGCACG TACCGIGIGG TCAGCGICCT CACCGICCTG CACCAGGACT GGCTGAATGG CAAGGAGTAC ACGGITCTGI ITCGGCGCCC ICCICGICAI GITGICGIGC AIGGCACACC AGTCGCAGGA GIGGCAGGA GIGGICCTGA CGACTIACC GITCCTCATG	2601 AAGTGCAAGG TCTCCAACAA AGCCCTCCCA GCCCCCATCG AGAAAACCAT CTCCAAAGCC AAAGGGCAGC CCCGAGAACC ACAGGTGTAC ACCCTGCCCC TTCACGTTCC AGAGGTTGTT TCGGGAGGGT CGGGGGTAGC TCTTTTGGTA GAGGTTTCGG TTTCCCGTCG GGGCTCTTGG TGTCCACATG TGGGACGGG 343 K C K V S N K A L P A P I E K T I S K A K G Q P R E P Q V Y T L P P	2701 CATCCCGGGA AGAGATGACC AAGAACCAGG TCAGCCTGAC CTGCCTGGTC AAAGGCTTCT ATCCCAGCGA CATGGCGTG GAGTGGGAGA GCAATGGGCA GTAGGGCCCT TCTCTACTGG TTCTTGGTCC AGTCGGACTG GACGGACCAG TTTCCGAAGA TAGGGTCGCT GTAGCGGCAC CTCACCCTCT CGTTACCGT 377 S R E E M T K N Q V S L T C L V K G F Y P S D I A V E W E S N G Q	2801 GCCGGAGAAC AACTACAAGA CCACGCCTCC CGTGCTGGAC TCCGACGGCT CCTTCTTCCT CTACAGCGAG CTCGCGTGG ACAAGAGCAG GTGGCAC CGCCCTCTG TTGATGTTCT GGTGCGGAGG GCACGACTG AGCTGCCGA GGAAGAAGGA GATGTCGTTC GAGTGGCACC TGTTCTCGTC CACCGTCGTC 410 P E N N Y K T T P P V L D S D G S F F L Y S K L T V D K S R W Q Q	2901 GGGAACGTCT TCTCATGCTC CGTGATGCAT GAGGCTCTGC ACAACCACTA CACGCAGAAG AGCCTCTCCC TGTCTCCGGG TAAATAAGCA TGCGACGGCC CCCTTGCAGA AGAGTACGAG GCACTACGTA CTCCGAGACG TGTTGGTGAT GTGCGTCTTC TGGAGAGGG ACAGAGGCCC ATTATTCGT ACGCTGCCGG 443 G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K O	3001 CTAGAGTCCC TAACGCTCGG TIGCCGCCGG GCGTTTTTA TIGTTAACTC ATGTTTGACA GCTTATCATC GATAAGCTTT AATGCGGTAG TTTATCACAG GATCTCAGGG ATTGCGAGCC AACGGCGGCC CGCAAAAAAT AACAATTGAG TACAAACTGT CGAATAGTAG CTATTCGAAA TTACGCCATC AAATAGTGTC	3101 TTAAATTGCT AACGCAGTCA GGCACCGTGT ATGAAATCTA ACAATGCGCT CATCGTCATC CTCGGCACCG TCACCCTGGA TGCTGTAGGC ATAGGCTTGG AATTTAACGA TTGCGTCAGT CCGTGGCACA TACTTTAGAT TGTTACGCGA GTAGCAGTAG GAGCCGTGGC AGTGGGACCT ACGACATCCG TATCCGAACC `Start Tet Resistance Coding	3201 TTATGCCGGT ACTGCCGGGC CTCTTGCGGG ATATCGTCCA TTCCGACAGC ATCGCCAGTC ACTATGGCGT GCTGCTAGCG CTATATGCGT TGATGCAATT AATACGGCCA TGACGGCCCG GAGAACGCCC TATAGCÀGGT AAGGCTGTCG TAGCGGTCAG TGATACCGCA CGACGATCGC GATATACGCA ACTACGTTAA
ACT TGA	700 J	0.000 >	100 A	999	TTT AAA	66 A))))))
SCAGG SGTCC Q D	CGAGA SCTCT R E	70000 \$6000	CACCG STGGC T v	TCTCC AGAGG S P	TAAGO	ACCC1 TGGGA	TGCTA
ου Συμ	ပိုဗိုင်	A C C L	ក្តី ក្តី	0 1 0 1 0 1 0 1 0 1 0 1 0 1 0 1 0 1 0 1	9 6	ი ეგ	ნ 4 ეე
TCCT(AGGA(L	66.76 06.70 0	AGCGU TCGC	GCAA CGTT	CTCC GAGG	TCAT	CACO	ეეეე ეეეე
CACCG GTGGC T	AAAGG TTTCC K G	ATCCC TAGGG	CTACA SATGT Y S	AGCCT TCGGA S L	GCTTA	CTCGG GAGCC ence	ACTAT
CCT GGA J		AGA	GGA J	TTC	ACA TGT	TAG	CAG
46061 7060A V 8	SGTTT	10000 10000 10000	rtctt vagað	SCCAC	STTTC	rcgrc Agcac ding	0600 30691
6 7 7 8 8 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	r CTC	5 € ×	000	A CAC	C ATC	4 6 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9 9	C AT
TGTG ACAC	ACCA TGGT	TGGT ACCA))))))	CACT GTGA H Y	AACT	GCGC	ACAG
TACCG ATGGC Y R	AGAAA TCTTT	CTGCC SACGG	TCCGA AGGCT S D	ACAAG TGTTG	TTGTT	AIGAAATCTA ACAAIGCGCT CATGGTCATC CTGG IACTITAGAI IOTIACGCGA GTAGCAGTAG GAGCG Start Tet Resistance Coding Sequence	TTCCG
ACG	AGC B	GAC	SGAC CTG	TGC SACG	TTA	CTA GAT Tet	rcca Agg T
ACAGO IGTOO	1000A 36661 P 1	AGCCT FCGGA	rgc TG ACGAC L	SGCTC SCGAG	STTTS	SAAAT CTTTA Cart	ATCGI TAGC
4 P	000 A	70 T T 70 Y 80 Y	6 6 7 8 8	T GA CTC	9 9	T ATC A TAC	S AT
CAGT.	TCCC. AGGG	CCAG GGTC O	CCTC GGAG	TGCA' ACGT	90090	CGTG	9909
GGAG CCTC	70000 10000 A L	AGAA TTCTT	CACG 3GTGC T	SCACT	TGCC	SGCAC	TCTT
ος υς υς ω	XX.	1001	& TOT	SAG C	000 J	407 607	ပ္ပပ္ပ
2000 2000 2000	CCAAC SGTTC N	GATG CTAC	TACA ATGT:	CATG GTACC	CGCTC	GCAG	9000
A TTT	TCT AGA S	AGA TCT	AA TTG	TCT AGA S	ATT	TTG	ACT TGA
AGACA CTGT	MAGG TTCC X V	GGGA SCCCT	AGAAC CTTG	CAGA	TCCC PAGGG	TTGCT	CGGGT
600A3 56611	AGTGC TCACG	ATCCC TAGGC S F	36CCT	GGAAC CCTTC N	TAGAC	TAAA1 ATTT?	TATGC
01 TK	43 T. Z.	10 10 10 10 10 10	, Q Q	ე . გენ	ខ្ម	2 F A	10 F 3
3 5	3 3	27	28	29	30	31	32

FIG. 10

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AGAGTCGAAT TCTCAGCTTA	CAGGTAGAGG GTCCATCTCC	CTCGTCAGTA GAGCAGTCAT	GTACGCAAGT CATGCGTTCA	A CGCTGATATC AT GCGACTATAG A D I Chain^	CTGAACTGGT GACTTGACCA L N W Y	GTTCTGGGAC CAAGACCCTG S G T	ACAGGGTACC TGTCCCATGG Q G T	GTGTGCCTGC CACACGGACG V C L L	AGGACAGCAA TCCTGTCGTT D S K	GGGCCTGAGC CCCGGACTCG G L S
AAAAAGAAGA TTTTTCTTCT	GTTGATTGAT CAACTAACTA	TTGAAGCATC AACTTCGTAG	TTTGTAACTA AAACATTGAT	CAAACGCG7 GTTTGCGC? N A Y art light	CAAGAGCTA GTTCTCGAI K S Y	TCTGGATCCG AGACCTAGGC S G S G	GGACATTTGG CCTGTAAACC T F G	TGCTTCTGTT ACGAAGACAA ASV	GTCACAGAGC CAGTGTCTCG V T E Q	TCACCCATCA AGTGGGTAGT T H Q
AAGCTTGCCC	ACCAACAGCG TGGTTGTCGC	AAAGAAGTTA TTTCTTCAAT	TTTTAATGTA AAAATTACAT	TCTATTGCT AGATAACGA S I A	GTCGCGACAT CAGCGCTGTA R D I	TTCTCGCTTC AAGAGCGAAG S R F	GAGTCTCCAT CTCAGAGGTA E S P W	AATCTGGAAC TTAGACCTTG S G T	CCAGGAGAGT GGTCCTCTCA Q E S	GCCTGCGAAG CGGACGCTTC A C E V
GTTGTTATTT	GCGCAAAATG CGCGTTTTAC	GCGATTACGT	TGTTTTTATT ACAAAAATAA	GTTCGTTTTT CAAGCAAAA F V F	TGCAGAGCCA ACGTCTCGGT C R A S	AAGGAGTCCC TTCCTCAGGG G V P	TCAGCACGGA AGTCGTGCCT Q H G	GAGCAGTTGA CTCGTCAACT E Q L K	CGGGTAACTC GCCCATTGAG G N S	CAAAGTCTAC GTTTCAGATG K V Y
TCATTGCTGA AGTAACGACT	TCGCAATATG AGCGTTATAC	GAGCTGCTGC	ATAGTCGCTT	TIGCAICTAI AACGIAGAIA A S M	CACCATCACC GTGGTAGTGG T I T	AGTCTCGCTG TCAGAGCGAC S L A E	ATTACTGTCT TAATGACAGA Y C L	GCCATCTGAT CGGTAGACTA P S D	GCCCTCCAAT CGGGAGGTTA A L Q S	ACGAGAAACA TGCTCTTTGT E K H
: ATGAAAATC	. CTGCAATGCT	. CGACGATACG	GCCGAGACTT CGGCTCTGAA	GAAAAACATC GCTTTTCTTC CTTTTTGTAG CGAAAAGAAG K N I A F L L STII signal TIR~2	GCGATAGGGT CGCTATCCCA D R V	CTATGCTACT GATACGATGA Y A T	TTCGCAACTT AAGCGTTGAA F A T Y	TCATCTTCCC AGTAGAAGGG I F P	GGTGGATAAC CCACCTATTG V D N	AAAGCAGACT TTTCGTCTGA K A D Y
AAATACAGAC	ATTATCGTCA TAATAGCAGT	GCATTCCTGA	AGTTGTCACG TCAACAGTGC	1)	GCCTCTGTGG CGGAGACACC A S V G	TACTGATTTA ATGACTAAAT L I Y	GCCAGAAGAC CGGTCTTCTG P E D	CCATCTGTCT GGTAGACAGA P S V F	TACAGTGGAA ATGTCACCTT Q W K	GACGCTGAGC CTGCGACTCG T L S
TCCATACT TTGGATAAGG	AGCTTTGGAG TCGAAACCTC	CCCGATGCCA GGGCTACGGT	GCTGTCATAA CGACAGTATT	GAATTATGAA C CTTAATACTT C M K ^start	CTCCCTGTCC GAGGGACAGG S L S	GCTCCGAAAG CGAGGCTTTC A P K V	GCAGTCTGCA CGTCAGACGT S L Q	TGTGGCTGCA ACACCGACGT V A A	GAGGCCAAAG CTCCGGTTTC E A K V	GCAGCACCCT CGTCGTGGGA S T L
TCTCCATACT AGAGGTATGA	CGCAGGTAGA GCGTCCATCT	CGAGGTAAAG GCTCCATTTC	CTTTTCAACA GAAAAGTTGT	AGGGTATCTA TCCCATAGAT	CAGATGACCC AGTCCCCGAG GTCTACTGGG TCAGGGGCTC Q M T Q S P S	ATCAACAGAAA ACCAGGAAAA TAGTIGICII IGGICCITITI Q Q K P G K	GGATTACACT CTGACCATCA CCTAATGTGA GACTGGTAGT D Y T L T I S	AAGGTGGAGA TCAAACGAAC TTCCACCTCT AGTTTGCTTG K V E I K R T	TGAATAACTT CTATCCCAGA ACTTATTGAA GATAGGGTCT N N F Y P R	GGACAGCACC TACAGCCTCA CCTGTCGTGG ATGTCGGAGT D S T Y S L S
GAATICAACT TC CTTAAGITGA AG	GAACTGTGTG CG CTTGACACAC GC	GGGCGCTGTA CG CCCGCGACAT GC	AAAAGTTAAT CT TTTTCAATTA GA	TCACGTAAAA AG AGTGCATTTT TC						1001 GGACAGCACC TACAGCCTCA CCTGTCGTGG ATGTCGGAGT 193 D S T Y S L S
1	101	201	301	401	501	601	701	801	901	1001

FIG. 2A

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GGGCCTGAGC CCCGGACTCG G L S	AGGCCTAACG TCCGGATTGC	TGCAATGCTT ACGTTACGAA	GACGATACGG CTGCTATGCC	CCGAGACTTA GGCTCTGAAT	CTTTTCTTCT GAAAGAAGA F L L TIR~2	CTCACTCCGT GAGTGAGGCA S L R	TTGATTGATC AACTAACTAG L I D P	TGAACAGCCT ACTTGTCGGA N S L	CTCGGCCTCC GAGCCGGAGG S A S	TTCCCCGAAC AAGGGGCTTG F P E P	GCAGCGTGGT CGTCGCACCA S V V
TCACCCATCA AGTGGGTAGT T H Q	CCGGGGGATCT GGCCCCTAGA	TTATCGTCAC AATAGCAGTG	CATTCCTGAC GTAAGGACTG	GTTGTCACGG	AAAACATCG (TTTTTGTAGC (K N I ASTII Signal	AGCCAGGGGG TCGGTCCCCC PGG	ATGGGTTGGA TACCCAACCT W V G	TACCTGCAGA ATGGACGTCT Y L Q M	TCACCGTCTC AGTGGCAGAG T V S	CAAGGACTAC GTTCCTGATG K D Y	TACTCCCTCA ATGAGGGAGT YSLS
GCCTGCGAAG CGGACGCTTC A C E V	AGCTCGGTAC TCGAGCCATG	GCTTTGGAGA CGAAACCTCT	CCGATGCCAG GGCTACGGTC	CTGTCATAAA GACAGTATTT	AATTATGAAG TTAATACTTC M K ^start	GGCCTGGTGC AGCCAGGGGG CCGGACCACG TCGGTCCCCC G L V Q P G G	AGGGCCTGGA TCCCGGACCT G L E	AAACACAGCA TTTGTGTCGT N T A	GGAACCCTGG TCACCGTCTC CCTTGGGACC AGTGGCAGAG G T L V T V S		CTCAGGACTC TACTCCCTCA GAGTCCTGAG ATGAGGGAGT S G L Y S L S
CAAAGICIAC GIIICAGAIG K V Y	carcgrggcg gragcaccgc	GCAGGTAGAA CGTCCATCTT	GAGGTAAAGC CTCCATTTCG	AAAGTTAATC TTTTCAACAG TTTCAATTAG AAAAGTTGTC	GGGTATCTAG CCCATAGATC	GTCTGGCGGT CAGACCGCCA S G G	GCCCCGGGTA CGGGGCCCAT A P G K		CTGGGGTCAA GACCCCAGTT WGQ	GCGGCCCTGG GCTGCCTGGT CGCCGGGACC: CGACGGACCA A A L G C L V	TCCTACAGTC AGGATGTCAG L Q S
AAAGCAGACT ACGAGAAACA TTTCGTCTGA TGCTCTTTGT K A D Y E K H	TAAATCCTCT ACGCCGGACG ATTTAGGAGA TGCGGCCTGC	AACTGTGTGC TTGACACACG	GGCGCTGTAC CCGCGACATG	TCGTCAGTAA AAAGTTAATC AGCAGTCATT TTTCAATTAG	CACGTAAAAA GTGCATTTTT	GCTGAGGTTC AGCTGGTGGA CGACTCCAAG TCGACCACCT A E V Q L V E ^start heavy chain	GGTCCGTCAG CCAGGCAGTC V R Q	ATAAGCGCTG TATTCGCGAC I S A D			TTCCCGGCTG TCCTACAGTC AAGGGCCGAC AGGATGTCAG F P A V L Q S
		ATCTCGAATG TAGAGCTTAC	AGGTAGAGGG TCCATCTCCC	TGAAGCATCC TCGTCAGTAA ACTTCGTAGG AGCAGTCATT	TACGCAAGTT ATGCGTTCAA	GCTGAGGTTC CGACTCCAAG A E V Q ^start h	ACATGCACTG TGTACGTGAC M H W	CCGTGCCACT GGCACGGTGA R A T	ACGGCCGCTT ACTTCGACTA TGCCGGCGAA TGAAGCTGAT T A A Y F D Y	CCCTCCTCCA AGAGCACCTC TGGGGGCACA GGGAGGAGGT TCTCGTGGAG ACCCCGTGT P S S K S T S G G T	CGTGCACACC GCACGTGTGG V H T
GACGCTGAGC CTGCGACTCG T L S	GAGTGTTAAT CTCACAATTA E C O	GCCGAĆGCGC CGGCTGCGCG	TTGATTGATC AACTAACTAG	TGAAGCATCC ACTTCGTAGG	TTGTAACTAG AACATTGATC	AAACGCGTAC TTTGCGCATG N A Y	AAGGAGTACT TTCCTCATGA K E Y Y	AGTTCCAGGA TCAAGGTCCT F Q D	TGCTCGAGAC ACGAGCTCTG A R D	CCCTCCTCCA GGGAGGAGGT PSSK	TGACCAGCGG ACTGGTCGCC T S G
GCAGCACCCT CGTCGTGGGA S T L	CAACAGGGA GTTGTCCCCT N R G	TTTTATTGTT AAAATAACAA	CCAACAGCGG GGTTGTCGCC	AAGAAGTTAT TTCTTCAATA	TTTAATGTAT AAATTACATA	CTATTGCTAC GATAACGATG I A T	CTTCAATATT GAAGTTATAA F N I	TATGACCCGA ATACTGGGCT Y D P K	TCTATTATTG AGATAATAAC Y Y C	CCCCCTGGCA GGGGGACCGT P L A	TCAGGCGCCC AGTCCGCGGG S G A L
GGACAGCACC TACAGCCTCA CCTGTCGTGG ATGTCGGAGT D S T Y S L S	CAAAGAGCTT GTTTCTCGAA K S F	GCCGGGCGTT	CGCAATATGG CGCAAAATGA GCGTTATACC GCGTTTTACT	CGATTACGTA GCTAATGCAT	GTTTTTATTT CAAAAATAAA	TTCGTTTTTT AAGCAAAAA F V F S	CAGCTTCTGG GTCGAAGACC A S G	CAACACGATC GTTGTGCTAG N T I	GACACTGCCG CTGTGACGGC D T A V	CATCGGTCTT GTAGCCAGAA S V F	GTCGTGGAAC CAGCACCTTG S W N
	TCGCCCGTCA AGCGGGCAGT S P V T	CTCGGTTGCC GAGCCAACGG	CGCAATATGG GCGTTATACC	AGCTGCTGCG TCGACGACGC	TAGTCGCTTT ATCAGCGAAA	TGCATCTATG ACGTAGATAC A S M	TTGTCCTGTG CAGCTTCTGG AACAGGACAC GTCGAAGACC L S C A A S G	CAGAGCAAGG GTCTCGTTCC E Q G	GCGTGCTGAG GACACTGCCG CGCACGACTC CTGTGACGGC R A E D T A V	ACCAAGGGCC CATCGGTCTT TGGTTCCCGG GTAGCCAGAA T K G P S V F	CGGTGACGGT GCCACTGCCA V T V
1001	1101	1201	1301	1401	1501	1601	1701	1801	1901	2001	2101

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101 (cggrgacggr gccacrgcca V T V	2101 CGGTGACGGT GTCGTGGAAC GCCACTGCCA CAGCACCTTG 177 V T V S W N	TCAGGCGCCC TGACCAGGGG AGTCCGCGGG ACTGGTCGCC S G A L T S G		CGTGCACC GCACGTGTGG V H T	TTCCCGGCTG AAGGGCCGAC F P A V		CTCAGGACTC GAGTCCTGAG S G L		GCAGCGTGGT CGTCGCACCA S V V
2201 0	GACTGTGCCC CTGACACGGG T V P	TCTAGCAGCT AGATCGTCGA S S S L	TGGGCACCCA ACCCGTGGGT G T Q	GACCTACATC CTGGATGTAG T Y I	TGCAACGTGA ACGTTGCACT C N V N	ATCACAAGCC TAGTGTTCGG H K P	CAGCAACACC GTCGTTGTGG S N T	AAGGTGGACA TTCCACCTGT K V D K	AGAAAGTTGA TCTTTCAACT K V E	GCCCAAATCT CGGGTTTAGA P K S
2301 7	TGTGACAAAA ACACTGTTTT C D K T	CTCACACATG GAGTGTGTAC H T C	CCCACCGTGC GGGTGGCACG P P C	CCAGCACCTG GGTCGTGGAC P A P E	AACTCCTGGG TTGAGGACCC L L G	GGGACCGTCA CCCTGGCAGT G P S		TCCCCCCAAA AGGGGGGTTT P P K	ACCCAAGGAC TGGGTTCCTG P K D	ACCCTCATGA TGGGAGTACT T L M I
2401 7	TCTCCCGGAC AGAGGGCCTG S R T	CCCTGAGGTC GGGACTCCAG P E V	ACATGCGTGG TGTACGCACC T C V V	rggrggacgr ACCACCTGCA V D V	GAGCCACGAA CTCGGTGCTT S H E	GACCCTGAGG CTGGGACTCC D P E V	TCAAGTTCAA AGTTCAAGTT K F N	CTGGTACGTG GACCATGCAC W Y V	GACGGCGTGG CTGCCGCACC D G V E	AGGTGCATAA TCCACGTATT V H N
310	TGCCAAGACA ACGGTTCTGT A K T	AAGCCGCGGG TTCGGCGCCC K P R E	AGGAGCAGTA TCCTCGTCAT E Q Y	CAACAGCACG GTTGTCGTGC N S T	TACCGTGTGG ATGGCACACC Y R V V	TCAGCGTCCT AGTCGCAGGA S V L	CACCGTCCTG GTGGCAGGAC T V L	CACCAGGACT GTGGTCCTGA H Q D W	GGCTGAATGG CCGACTTACC L N G	CAAGGAGTAC GTTCCTCATG K E Y
2601 7 343 P	AAGTGCAAGG TTCACGTTCC K C K V	AAGTGCAAGG TCTCCAACAA TTCACGTTCC AGAGGTTGTT K C K V S N K	AGCCCTCCCA TCGGGAGGGT A L P	GCCCCCATCG CGGGGGTAGC A P I E	AGAAAACCAT TCTTTTGGTA K T I	CTCCAAAGCC GAGGTTTCGG S K A	AAAGGGCAGC TTTCCCGTCG K G Q P	CCCGAGAACC GGGCTCTTGG R E P	ACAGGTGTAC TGTCCACATG Q V Y	ACCCTGCCCC TGGGACGGG
2701 (2701 (377	CATCCCGGGA GTAGGGCCCT S R E	CATCCCGGGA AGAGATGACC GTAGGGCCT TCTCTACTGG S R E E M T		TCAGCCTGAC AGTCGGACTG S L T	CTGCCTGGTC GACGGACCAG C L V	AAAGGCTÍCT TITCCGAAGA K G F Y	ATCCCAGCGA TAGGGTCGCT P S D	CATCGCCGTG GTAGCGGCAC I A V	GAGTGGGAGA CTCACCCTCT E W E S	GCAATGGGCA CGTTACCCGT N G Q
2801 0	GCCGGAGAAC CGGCCTCTTG P E N	AACTACAAGA TTGATGTTCT N Y K T	CCACGCCTCC GGTGCGGAGG T P P	CGTGCTGGAC GCACGACCTG V L D	TCCGACGGCT AGGCTGCCGA S D G S	CCTTCTTCCT GGAAGAAGGA F F L	CTACAGCAAG GATGTCGTTC YSK		CTCACCGTGG ACAAGAGCAG GAGTGGCACC TGTTCTCGTC L T V D K S R	GTGGCAGCAG CACCGTCGTC W Q Q
2901 (GGGAACGTCT CCCTTGCAGA G N V F	GGGAACGTCT TCTCATGCTC CCCTTGCAGA AGAGTACGAG G N V F S C S	CGTGATGCAT GCACTACGTA V M H	GAGGCTCTGC CTCCGAGACG E A L H	ACAACCACTA TGTTGGTGAT N H Y	CACGCAGAAG GTGCGTCTTC T Q K	AGCCTCTCCC TCGGAGAGGG S L S L	TGTCTCCGGG ACAGAGGCCC S P G	TAAATAAGCA ATȚTATTCGT K O	TGCGACGGCC ACGCTGCCGG
3001 (CTAGAGTCCC GATCTCAGGG	TAACGCTCGG ATTGCGAGCC	TTGCCGCCGG	GCGTTTTTTA CGCAAAAAT	TTGTTAACTC AACAATTGAG	ATGTTTGACA TACAAACTGT	GCTTATCATC	GATAAGCTTT CTATTCGAAA	AATGCGGTAG TTACGCCATC	tttatcacag aaatagtgtc
3101 3	TTAAATTGCT AATTTAACGA	AACGCAGTCA TTGCGTCAGT	. GGCACCGTGT	ATGAAATCTA TACTTTAGAT	ACAATGCGCT TGTTACGCGA	CATCGTCATC GTAGCAGTAG	CTCGGCACCG	TCACCCTGGA	TGCTGTAGGC ACGACATCCG	ATAGGCTTGG TATCCGAACC
3201	TTATGCCGGT AATACGGCCA	ACTGCCGGGC TGACGGCCCG	TTATGCCGGT ACTGCCGGGC CTCTTGCGGG AATACGGCCA TGACGGCCCG GAGAACGCCC	ATATCGTCCA TT TATAGCAGGT AA	TT AA					

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AGAGTCGAAT TCTCAGCTTA	CAGGTAGAGG GTCCATCTCC	CTCGTCAGTA GAGCAGTCAT	GFACGCAAGT CATGCGTTCA	cgcrgararc 3cgacrarag A D I hain^	AAACTGGT \TTTGACCA N W Y	GTTCTGGGAC CAAGACCCTG S G T	ACAGGGTACC TGTCCCATGG Q G T	GTGTGCCTGC CACACGGACG V C L L	AGGACAGCAA TCCTGTCGTT D S K	GGGCCTGAGC CCCGGACTCG G L S	AGGCCTAACG TCCGGATTGC
	GTTGATTGAT CAGGTAGAGG CAACTAACTA GTCCATCTCC	TTGAAGCATC AACTTCGTAG		GAATTATGAA GAAGAATATC GCATTTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGCGTA CGCTGATATC CTTAATACTT CTTCTTATAG CGTAAAGAAG AACGTAGATA CAAGCAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG M K K N I A F L L A S M F V F S I A T N A Y A D I ^STII Signal TIR -1	GCGATAGGGT CACCATCACC TGCAGCGCAA GTCAGGATAT TAGCAACTAT TTAAACTGGT CGCTATCCCA GTGGTAGTGG ACGTCGCGTT CAGTCCTATA ATCGTTGATA AATTTGACCA D R V T I T 'C S A S Q D I S N Y 'L N W Y	TCTGGATCCG GT AGACCTAGGC CA S G S G		TGCTTCTGTT GTC ACGAAGACAA CAC A S V V			1101 TCGCCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTTAAT TAAATCCTCT ACGCCGGACG CATCGTGGCG AGCTCGGTAC CCGGGGATCT AGGCCTAACG AGCGGGCAGT GTTTCTCGAA GTIGTCCCCT CTCACAATTA ATTTAGGAGA TGCGGCCTGC GTAGCACCGC TCGAGCCATG GGCCCCTAGA TCCGGAITGC 238 & B.V.T. K.S.B.N.B.C.E.C.G.E.C.C.C.C.C.C.C.C.C.C.C.C.C.C.C
GAATICAACT TCTCCATACT TIGGATAAGG AAATACAGAC AIGAAAAATC TCATIGCIGA GITGTIATIT AAGCTIGCCC AAAAAGAAGA CTIAAGTIGA AGAGGIAIGA AACCTATICC TITATGICIG TACTITITAG AGTAACGACT CAACAATAAA TICGAACGGG TITITCTICT	GAACTGIGIG GGCAGGIAGA AGCITIGGAG AITAICGICA CIGCAAIAGCI ICGCAAIAIG GCGCAAAAIG ACCAACAGCG CITGACACAC GCGICCAICI ICGAAACCIC IAAIAGCAGI GACGIIACGA AGCGIIAIAC GGCGIIIIIAC IGGIIGICGC	GGGGGGTGTA CGAGGTAAAG CCGGATGCCA GCATTCCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA CCCGGGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT	301 AAAAGTTAAT CTTITCAACA GCIGICATAA AGTIGICACG GCCGAGACTI AIAGIGGCIT IGITITIATI IITTAAIGIA IIIGIAACIA ITTICAATTA GAAAAGTIGI CGACAGIAIT ICAACAGIGC GGGCICIGAA IAICAGCGAA ACAAAAATA AAAAITACAI AAACAIIGAT	TCTATTGCTA AGATAACGAT S I A T Anti-V	CTCCCTGTCC GCCTCTGTGG GCGATAGGGT CACCATCACC TGCAGCGCAA GTCAGGATAT / GAGGGACAGG CGGAGACAC CGCTATCCCA GTGGTAGTGG ACGTCGCGTT CAGTCCTATA / S L S A S V G D R V T I T 'C S A S Q D I	GCTCCGAAAG TACTGATTTA CTTCACCTCC TCTCTCCACT CTGGAGTCCC TTCTCGCTTC TCTGGATCCC CGAGGCTTTC ATGACTAAAT GAAGTGGAGG AGAGAGGTGA GACCTCAGGG AAGAGGAGA AGACTTAGGC A P S R F S G S G	CTGACCATCA GCAGICIGCA GCCAGAAGAC ITCGCAACTI ATTACIGICA ACAGIAIAGC ACCGIGCCGI GGACGITIGG GACTGGIAGI CGICAGACGI CGGICTICIG AAGCGIIGAA IAAIGACAGI IGICAIAICG IGGCACGGCA CCIGCAAACC L I I S S L Q P E D F A I Y Y C Q Q Y S I V P W I F G	AATCTGGAAC 1 TTAGACCTTG A S G T	GGTGGATAAC GCCCTCCAAI CGGGTAACTC CCAGGAGAGT GTCACAGAGC CCACCTATIG CGGGAGGTTA GCCCATTGAG GGTCCTCTCA CAGTGTCTCG V D N A L Q S G N S Q E S V T E Q	GGACAGCACC TACAGCCTCA GCAGCACCCT GACGCTGAGC AAAGCAGAACA ACGAGAAACA CAAAGTCTAC GCCTGCGAAG TCACCCATCA CCTGTCGTGG ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT GTTTCAGATG CGGACGCTTC AGTGGGTAGT D S T Y S L S S T L T L S K A D Y È K H K V Y A C E V T H Q	TCGCCCGTCA CAAAGAGCTT CAACAGGGGA GAGTGTTAAT TAAATCCTCT ACGCCGGACG CATCGTGGCG AGCTCGGTAC CCGGGGATCT AGCGGGCAGT GTITCTCGAA GTIGTCCCCT CTCACAATTA ATTTAGGAGA TGCGGCCTGC GTAGCACCGC TCGAGCCATG GGCCCTAGA S
GTTGTTATTT CAACAATAAA	GCGCAAAATG CGCGTTTTAC	GCGATTACGT CGCTAATGCA	TGTTTTTATT ACAAAAATAA	GTTCGTTTTT CAAGCAAAA F V F	C TGCAGCGCAA B ACGTCGCGTT C S A S	CTGGAGTCCC GACCTCAGGG	ACAGTATAGC TGTCATATCG Q Y S	GAGCAGTIGA CTCGTCAACT E Q L K	CGGGTAACTC. GCCCATTGAG G N S	CAAAGTCTAC GITTCAGAIG K V Y	CATCGTGGCG ,
TCATTGCTGA AGTAACGACT	TCGCAATATG AGCGTTATAC	GAGCTGCTGC CTCGACGACG	ATAGTCGCTT TATCAGCGAA	GCATTTCTTC TTGCATCTAT CGTAAAGAAG AACGTAGATA A F L L A S M -1	CACCATCACC GTGGTAGTGG T I T T	TCTCTCCACT AGAGAGGTGA S L H S	ATTACTGTCA TAATGACAGT Y C Q	GCCATCTGAT GAGCAGTTGA AATCTGGAAC CGGTAGACTA CTCGTCAACT TTAGACCTTG P S D E Q L K S G T	GCGCTCCAAT CGGGAGGTTA A L Q S	ACGAGAAACA TGCTCTTTGT È K H	ACGCCGGACG (
TACTITITAG	CTGCAATGCT GACGTTACGA	CGACGATACG GCTGCTATGC	GCCGAGACTT CGGCTCTGAA	GCATTTCTTC CGTAAAGAAG A F L L	GCGATAGGGT CGCTATCCCA D R V	CTTCACCTCC GAAGTGGAGG F T S	GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTCA ACAGTATAGC ACCGTGCCGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAGT TGTCATATCG TGGCACGGCA S L Q P E D F A T Y Y C Q Q Y S T V P W		GGTGGATAAC CCACCTATTG V D N	AAAGCAGACT TTTCGTCTGA K A D Y	TAAATCCTCT ATTTAGGAGA
AAATACAGAC TTTATGTCTG	ATTATCGTCA TAATAGCAGT	GCATTCCTGA CGTAAGGACT	AGTTGTCACG TCAACAGTGC	ATGAA GAAGAATATC GC) TACTI CTTCTTATAG CG; M K K N I A ^STII Signal TIR -1	CTCCCTGTĆC GCCTCTGTGG GAGGGACAGG CGGAGACACC S L S A S V G	GCTCCGAAAG TACTGATTTA CGAGGCTTTC ATGACTAAAT A P K V L I Y	GCCAGAAGAC CGGTCTTCTG P E D	CCATCTGTCT TCATCTTCCC GGTAGACAGA AGTAGAAGGG P S V F I F P	GAGGCCAAAG TACAGTGGAA GGTGGATAAC CTCCGGTTTC ATGTCACCTT CCACCTATTG E A K V D W K V D N	GACGCTGAGC CTGCGACTCG T L S	GAGTGTTAAT CTCACAATTA
TIGGATAAGG	AGCTTTGGAG	CCCGATGCCA GGGCTACGGT	GCTGTCATAA CGACAGTATT	GAATTATGAA CTTAATACTT M K ^STII	CTCCCTGTĆC GAGGGACAGG S L S		GCAGTCTGCA CGTCAGACGT S L Q	TGTGGCTGCA ACACCGACGT V A A	GAGGCCAAAG TACAGTGGAA CTCCGGTTTC ATGTCACCTT E A K V Q W K	GCAGCACCT GACGCTGAGC CGTCGTGGGA CTGCGACTCG S T L T L S	CAACAGGGGA GITGICCCCI
TCTCCATACT	GCGAGGTAGA	CGAGGTAAAG GCTCCATTTC	AAAAGTTAAT CTTTTCAACA TTTTCAATTA GAAAAGTTGT	AGGGTATCTA TCCCATAGAT	CAGTIGACCC AGICCCCGAG GICAACIGG ICAGGGGCIC Q L I Q S R S	ACCAGGAAAA TGGTCCTTTT P G K	CTGACCATCA GACTGGTAGT L T I S	AAGGIGGAGA TCAAACGAAC TGIGGCTGCA TTCCACCTCT AGTTTGCTTG ACACCGACGT K V E I K R T V A A	CTATCCCAGA GATAGGGTCT Y P R	TACAGCCTCA ATGTCGGAGT Y S L S	CAAAGAGCTT GTTTCTCGAA
CTTAAGTTGA	GAACTGTGTG	201 GGGCGCTGTA CCCGCGACAT	AAAAGTTAAT TTTTCAATTA	401 TCACGTAAAA AGGGTATCTA AGTGCATTTT TCCCATAGAT 1		601 ATCAACAGAA ACCAGGAAAA TAGTTGTCTT TGGTCCTTTT 60 Q Q K P G K	701 GGATTTCACT CCTAAAGTGA 93 D F T		901 TGAATAACTT CTATCCCAGA ACTTATTGAA GATAGGGTCT 160 N N F Y P R	GGACAGCAC TACAGCCTCA CCTGTCGTGG ATGTCGGAGT D S T Y S L S	TCGCCCGTCA CAAAGAGCTT CAACAGGGAAAGGGGAAGGGGAGT GTTCTCGAA GTTGTCCCCT
	101	201	301	401	501	601	701	801	901	1001	1101

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1201		CTCGGTTGCC GCCGGGCGTT TTTTATTGTT GAGCCAACGG CGGCCGCAA AAAATAACAA	GCCGGCGTT TITIATTGTT CGGCCCGCAA AAAATAACAA	GCCGACGCGC	GCCGACGCGC ATCTCGAATG CGGCTGCGCG TAGAGCTTAC	GCCGACGCGC ATCTCGAATG AACTGTGTGC GCAGGTAGAA GCTTTGGAGA TTATCGTCAC TGCAATGCTT CGGCTGCGCG TAGAGCTTAC TTGACACACG CGTCCATCTT CGAAACCTCT AATAGCAGTG ACGTTACGAA	GCAGGTAGAA CGTCCATCTT	GCTTTGGAGA	TTATCGTCAC AATAGCAGTG	TTATCGTCAC TGCAATGCTT AATAGCAGTG ACGTTACGAA
1301	1 CGCAATATGG GCGTTATACC	G CGCAAAATGA C GCGTTTTACT	CCAACAGCGG	TTGATTGATC AACTAACTAG	AGGTAGAGGG TCCATCTCCC	GGCGCTGTAC	GAGGTAAAGC CTCCATTTCG	CCGATGCCAG	CATTCCTGAC GTAAGGACTG	GACGATACGG CTGCTATGCC
1401	1 AGCTGCTGCG TCGACGACGC	G CGATTACGTA C GCTAATGCAT		AAGAAGITAT IGAAGCAICC ICGICAGIAA IICTICAAIA ACTICGIAGG AGCAGICAIT	TCGTCAGTAA AGCAGTCATT		AAAGITAATC TTTTCAACAG CTGTCATAAA TTTCAATTAG AAAAGTTGTC GACAGTATTT	CTGTCATAAA GACAGTATTT	GTTGTCACGG	CCGAGACTTA GGCTCTGAAT
1501	1 TAGTCGCTTT ATCAGCGAAA 1	I GITITIAITI A CAAAATAAA	TTTAATGTAT AAATTACATA	TTGTAACTAG AACATTGATC	TTGTAACTAG TACGCAAGTT AACATTGATC ATGCGTTCAA	CACGTAAAAA GTGCATTTT	GGGTATCTAG CCCATAGATC	AATTATGAAG TTAATACTTC M K ^ STII	AATTATGAAG AAGAATATCG TTAATACTTC TTCTTATAGC M K K N I A STII Signal TIR-1	CATTTCTTCT GTAAAGAAGA F L L
1601	1601 TGCATCTATG ACGTAGATAC 10 A S M	S TTCGITTITT C AAGCAAAAA F V F S	CTATTGCTAC GATAACGATG I A T	AAACGCGTAC TTTGCGCATG N A Y	GCT CGA A	AGCTGGTGGA TCGACCACCT L V E GF Heavy Ch	TGGCGGT ACCGCCA G G	GGCCTGGTGC CCGGACCACG G L V Q	GGCCTGGTGC AGCCAGGGGG CCGGACCACG TCGGTCCCC G L V Q P G G	CTCACTCCGT GAGTGAGGCA S L R
1701	1 TTGTCCTGTG AACAGGACAC 3 L S C A	G CAGCTTCTGG C GTCGAAGACC A A S G	CTACGACTTC GATGCTGAAG Y D F.	ACGCACTACG TGCGTGATGC T H Y G	GTATGAACTG CATACTTGAC M N W	GGTCCGTCAG CCAGGCAGTC V R Q	GCCCCGGGTA CGGGGCCCAT A P G K	AGGGCCTGGA TCCCGGACCT G L E	ATGGGTTGGA TACCCAACCT W V G	TGGATTAACA ACCTAATTGT W I N T
1801	1 CCTATACCGG. GGATATGGCC 7 Y T G	S. TGAAÓCGACC C. ACTTGGCTGG E. P. T	TATGCTGCGG ATACGACGCC Y A A D	ATTTCAAACG TAAAGTTTGC F K R	TCGTTTCACT AGCAAAGTGA R F T	TTTTCTTTAG AAAAGAAATC F S L D	ACACCTCCAA TGTGGAGGTT T S K	AAGCACAGCA TTCGTGTCGT S T A	TACCTGCAGA ATGGACGTCT Y L Q M	TGAACAGCCT ACTTGTCGGA N S L
1901	1 GCGCGCTGAG CGCGCGACTC 0 R A E	S GACACTGCCG C CTGTGACGCC D T A V	TCTATTACTG AGATAATGAC Y Y C	TGCAAAGTAC ACGTTTCATG A K Y	CCGTACTATT GGCATGATAA P Y Y Y	ACGGCACGAG TGCCGTGCTC G T S	CCACTGGTAT GGTGACCATA H W Y	TTCGACGTCT AAGCTGCAGA F D V W	GGGGTCAAGG CCCCAGTTCC G Q G	AACCCTGGTC TTGGGACCAG T L V
2001	1 ACCGTCTCCT TGGCAGAGGA 3 T V S S	r ceeccrccac A ecceeaegre	CAAGGGCCCA GTTCCCGGGT K G P	TCGGTCTTCC AGCCAGAAGG S V F P	CCCTGGCACC GGGACCGTGG L A P	CTCCTCCAAG GAGGAGGTTC S S K	AGCACCTCTG TCGTGGAGAC S T S G	GGGCACAGC CCCCGTGTCG G T A	GGCCCTGGGC CCGGGACCCG A L G	TGCCTGGTCA : ACGGACCAGT C L V K
2101	1 AGGACTACTT TCCTGATGAA 7 D Y F	r ccccgaaccg a ggggcrrggc P E P	GTGACGGTGT CACTGCCACA V T V S	CGTGGAACTC GCACCTTGAG W N S	AGGCGCCCTG TCCGCGGGAC G A L	ACCAGCGGCG TGGTCGCCGC T S G V	TGCACACCTT ACGTGTGGAA H T F	CCCGGCTGTC GGGCCGACAG P A V	CTACAGTCCT GATGTCAGGA L Q S S	CAGGACTCTA GTCCTGAGAT G L Y
2201	CTCCCTCAGC GAGGGAGTCG	AGCGTGGTGA TCGCACCACT S V V T	CTGTGCCCTC GACACGGGAG V P S	TAGCAGCTTG ATCGTCGAAC S S L	GGCACCCAGA CCGTGGGTCT G T Q T	CCTACATCTG GGATGTAGAC Y I C	CAACGTGAAT GTTGCACTTA N V N	CACAAGCCCA GTGTTCGGGT H K P S	GCAACACCAA CGTTGTGGTT N T K	GGTGGACAAG CCACCTGTTC ' D K
2301	1 AAAGTTGAGC TTTCAACTCG 3 K V E P	CCAAATCTTG GGTTTAGAAC K S C	TGACAAAACT ACTGTTTTGA D K T	CACACATGCC GTGTGTACGG H T C P	CACCGIGCCC GIGGCACGGG P C P	AGCACCTGAA TCGTGGACTT A P E	CTCCTGGGGG GAGGACCCCC	GACCGTCAGT CTGGCAGTCA P S V	CTTCCTCTTC GAAGGAGAAG F L F	CCCCCAAAAC GGGGGTTTG P P K P
2401	1 CCAAGGACAC .GGTTCCTGTG 7 K D T	CCTCATGATC GGAGTACTAG L M I	TCCCGGACCC AGGGCCTGGG S R T P	CTGAGGTCAC GACTCCAGTG E V T	ATGCGTGGTG TACGCACCAC	GTGGACGTGA CACCTGCACT V D V S		CCCTGAGGTC AAGTTCAACT GGGACTCCAG TTCAAGTTGA P E V K F N W		GGTACGTGGA CCATGCACCT Y V D

FIG. 3B

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AGGACTGG TCCTGACC D W	AGAACCAC TCTTGGTG E P Q	GCCGTGGA CGGCACCT A V E	CCGTGGAC GGCACCTG	TCCGGGTA SAGGCCCAT P G K	AGCTTTAA TTCGAAATT	CCTGGATG	SCTAGCGCT SGATCGCGA
2501 CGGCGTGGAG GTGCATAATG CCAAGACAAA GCCGCGGGAG GAGCAGTACA ACAGCACGTA CCGTGTGGTC AGCGTCCTCA CCGTCCTGCA CCAGACTGG GCCGCACCTC CACGTATTAC GGTTCTGTTT CGGCGCCCTC CTCGTCATGT TGTCGTGCAT GGCACACCAG TCGCAGGAGT GCCAGGACGT GGTCCTGACC 310 G V E V H N A K T K P R E E Q Y N S T Y R V V S V L T V L H Q D W	2601 CTGNATGGCA AGGAGTACAA GTGCAAGGTC TCCAACAAAG CCCTCCCAGC CCCCATCGAG AAAACCATCT CCAAAGGCAAA AGGGCAGCCC CGAGAACCAC GACTTACCGT TCCTCATGTT CACGTTCCAG AGGTTGTTTC GGGAGGGTGG GGGTAGCTC TTTTGGTAGA GGTTTCGGTT TCCCGTCGG GCTCTTGGTG 343 L N G K E Y K C K V S N K A L P A P I E K T I S K A K G O P R E P O	2701 AGGTGTACAC CCTGCCCCCA TCCCGGGAAG AGATGACCAA GAACCAGGTC AGCCTGACCT GCCTGGTCAA AGGCTTCTAT CCCAGCGACA TCGCCGTGGA TCCACATGTG GGACGGGGGT AGGGCCCTTC TCTACTGGTT CTTGGTCCAG TCGGACTGGA CGGACCAGTT TCCGAAGATA GGGTCGCTGT AGCGGCACCT 377 v y t L p p s r e e m t k n q v s l t c l v k g f y p s D i a v e	2801 GTGGGAGAGC AATGGGCAGC CGGAGAACAA CTACAAGACC ACGCCTCCCG TGCTGGACTC CGACGGCTCC TTCTTCCTCT ACAGCAAGCT CACCGTGGAC CACCCTCTCG TTACCCGTCG GCCTCTTGTT GATGTTCTGG TGCGGAGGGC ACGACCTGAG GCTGCCGAGG AAGAAGGAGA TGTCGTTCGA GTGGCACCTG	2901 AAGAGCAGGT GGCAGCAGGG GAACGTCTTC TCATGCTCCG TGATGCATGA GGCTCTGCAC AACCACTACA CGCAGAAGAG CCTCTCCCTG TCTCCGGGTA TTCTCGTCCA CCGTCGTCCC CTTGCAGAAG AGTACGAGGC ACTACGTACT CCGAGACGTG TTGGTGATGT GCGTCTTCTC GGAGAGGGAC AGAGGCCCAT 443 K S R W Q Q G N V F S C S V M H E A L H N H Y T Q K S L S L S P G K	3001 AATAAGCATG CGACGGCCCT AGAGTCCCTA ACGCTCGGTT GCCGCCGGGC GTTTTTTATT GTTAACTCAT GTTTGACAGC TTATCATCGA TAAGCTTTAA TTATTCGTAC GCTGCCGGGA TCTCAGGGAT TGCGAGCCAA CGGCGGCCCG CAAAAAATAA CAATTGAGTA CAAACTGTCG AATAGTAGCT ATTCGAAATT 477 O	3101 IGCGGIAGIT TATCACAGIT AAATIGCIAA CGCAGICAGG CACCGIGIAT GAAAICIAAC AAIGCGCICA ICGICAICCI CGGCACCGIC ACCCIGGAAG ACGCCAICAA ATAGIGICAA ITIAACGAIT GCGICAGICC GIGGCACAIA CITIAGAIIG ITACGCGAGI AGCAGIAGGA GCCGIGGCAG IGGGACCIAC	3201 CTGTAGGCAT AGGCTTGGTT ATGCCGGTAC TGCCGGGCCT CTTGCGGGAT ATCGTCCATT CCGACAGCAT CGCCAGTCAC TATGGCGTGC TGCTAGCGCT GACATCCGTA TCCGAACCAA TACGGCCATG ACGCCCCGGA GAACGCCCTA TAGCAGGTAA GGCTGTCGTA GCGGTCAGTG ATACCGCACG ACGATCGCGA
AGCGTCCTCA TCGCAGGAGT S V L T	CCAAAGCCAA GGTTTCGGTT K A K	AGGCTTCTAT TCCGAAGATA G F Y	TTCTTCCTCT AAGAAGGAGA F F L Y	CGCAGAAGAG GCGTCTTCTC Q K S	GTTTGACAGC	AT GAAATCTAAC AATGGGTCA TCGTCATCCT CO TA CTTTAGATTG TTACGCGAGT AGCAGTAGGA GO Start Tet Resistance Coding Sequence	CGCCAGTCAC
CCGTGTGGTC GGCACACCAG R V V	AAAACCATCT TTTTGGTAGA K T I S	GCCTGGTCAA CGGACCAGTT L V K	CGACGGCTCC GCTGCCGAGG D G S	AACCACTACA TTGGTGATGT N H Y T	GTTAACTCAT CAATTGAGTA	AATGCGCTCA TTACGCGAGT sistance Coo	CCGACAGCAT
ACAGCACGTA TGTCGTGCAT S T Y	CCCCATCGAG GGGGTAGCTC P I E	AGCCTGACCT TCGGACTGGA S L T C	TGCTGGACTC ACGACCTGAG L D S	GGCTCTGCAC CCGAGACGTG A L H	GTTTTTATT CAAAAATAA	GAAATCTAAC CTTTAGATTG tart Tet Re	ATCGTCCATT TAGCAGGTAA
GAGCAGTACA CTCGTCATGT E Q Y N	CCCTCCCAGC GGGAGGGTCG L P A	GAACCAGGTC CTTGGTCCAG N Q V	ACGCCTCCCG TGCGGAGGGC T P P V	TGATGCATGA ACTACGTACT M H E	ອວວວອອວອວ ວອອອວວອວວອ	CACCGTGTAT GTGGCACATA S	CTTGCGGGAT GAACGCCCTA
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CCAAGACAAA GGTTCTGTTT K T K	GTGCAAGGTC CACGTTCCAG C K V	TCCCGGGAAG AGGGCCCTTC S R E E	CGGAGAACAA GCCTCTTGTT E N N	GAACGTCTTC CTTGCAGAAG N V F	AGAGTCCCTA TCTCAGGGAT	AAATTGCTAA TTTAACGATT	ATGCCGGTAC TACGGCCATG
GTGCATAATG CACGTATTAC V H N A	AGGAGTACAA TCCTCATGTT E Y K	CCTGCCCCA GGACGGGGGT L P P	AATGGGCAGC TTACCCGTCG N G Q P	GGCAGCAGGG CCGTCGTCCC Q Q G	CGACGGCCCT	TATCACAGTT ATAGTGTCAA	AGGCTTGGTT TCCGAACCAA
CGGCGTGGAG GCCGCACCTC G V E	CTGAATGGCA GACTTACCGT L N G K	AGGTGTACAC TCCACATGTG V Y T	GTGGGAGAGC CACCCTCTCG W E S	AAGAGCAGGT TTCTCGTCCA K S R W	AATAAGCATG TTATTCGTAC O	TGCGGTAGTT ACGCCATCAA	CTGTAGGCAT GACATCCGTA
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	AATTTGACCA L N W Y	ATCGTTGATA S N Y	GTCAACTGGG TCAGGGGCTC GAGGGACAGG CGGAGACACC CGCTATCCCA GTGGTAGTGG ACGTCGCGTT CAGTCCTATA ATCGTTGATA AATTTGACCA Q L T Q S P S S L S A S V G D R V T I T C S A S Q D I S N Y L N W Y	AČGTCGCGTT C S A S	GTGGTAGTGG T I T	CGCTATCCCA D R V	CGGAGACACC A S V G	GAGGGACAGG S L S	TCAGGGGCTC S P S	GTCAACTGGG TCAGGG 26 Q L T Q 'S P	26
chai	Light chair TTAAACTGGT	TAGCAACTAT	GTCAGGATAT	TGCAGCGCAA	CACCATCACC	GCGATAGGGT	GCCTCTGTGG	crecereree	AGTCCCCGAG	LIGHT. 501 CAGTIGACCC AGICCCCGAG CICCCIGICC GCCICIGIGG GCGAIAGGGI CACCAICACC IGCAGCGCAA GICAGGAIAI IAGCAACTAI ITAAACIGGI	501
- ا ا	CGCTGATATC GCGACTATAG A D I	CAAACGCGTA GTTTGCGCAT N A Y	GAATTATGAA GAAGAATATC GCATTTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGCGTA CGCTGATATC CTTAATACTT CTTCTTATAG CGTAAAGAAG AACGTAGATA CAAGCAAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG M 'K K N I A F L L A S M F V F S I A T N A Y A D I ^STII Signal TIR ~1	GTTCGTTTTT CAAGCAAAAA F V F	TIGCATCIAT AACGTAGATA A S M	GCATTTCTTC CGTAAAGAAG A F L L	ATGAA GAAGAATATC GC. TACTT CTTCTTATAG CG' M 'K K N I A ^STII Signal TIR ~1	GAATTATGAA CTTAATACTT M 'K ^STII	TCACGTAAAA AGGGTATCTA AGTGCATTTT TCCCATAGAT	401 TCACGTAAAA AGGGTATCTA GAATTATGAA GAAGAATATC GCATTTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGCGTA CGCTGATATC AGTGCATTTT TCCCATAGAT CTTAATACTT CTTCTTATAG CGTAAAGAAG AACGTAGATA CAAGCAAAAA AGATAACGAT GTTGCGCAT GCGACTATAG 1 1 1 1 2 1 2 2 1 3 1 1 1 1 2 2 1 1 2 1 2	401 1
	GTACGCAAGT CATGCGTTCA	TTTGTAACTA AAACATTGAT	AAAAGITAAT CITITCAACA GCTGICATAA AGITGICACG GCCGAGACIT AIAGICGCIT IGITITIAIT ITITAAGTA TITGIAACIA GIACGCAAGI ITIICAAITA GAAAAGIIGI CGACAGIAII ICAACAGIGC CGGCICTGAA TAICAGCGAA ACAAAAITA AAAAITACAI AAACAITGAI CAIGCGIICA	TGTTTTTATT ACAAAAATAA	ATAGTCGCTT TATCAGCGAA	GCCGAGACTT CGGCTCTGAA	AGTTGTCACG TCAACAGTGC	GCTGTCATAA CGACAGTATT	CTTTTCAACA GAAAAGTTGT	301 AAAAGITAAT CITITCAACA GCTGTCATAA AGTTGTCACG GCCGAGACTT ATAGTCGCTT TGTTTTTATT TTTTAATGTA TTTGTAACTA GTACGCAAGT TTTTCAATTA GAAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA	301
	CTCGTCAGTÅ GAGCAGTCAT	TTGAAGCATC	GGGCGCTGTA CGAGGTAAAG CCCGATGCCA GCATTCCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTCAGTA CCCGCGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT	GCGATTACGT CGCTAATGCA	GAGCTGCTGC CTCGACGACG	CGACGATACG GCTGCTATGC	GCATTCCTGA CGTAAGGACT	CCCGATGCCA GGGCTACGGT	CGAGGTAAAG GCTCCATTTC	201 GGGCGCTGTA CGAGGTAAAG CCCGATGCCA GCATTCCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTCAGTA CCCGCGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT	201
	CAGGTAGAGG GTCCATCTCC	GTTGATTGAT	gaactgigtg cgcaggtaga agctitiggag attatcgtca ctgcaatgct tcgcaatatg gcgcaaaatg accaacagcg gttgattgat caggtagagg Cttgacacac gcgtccatct tcgaaacctc taatagcagt gacgttacga agcgttatac cgcgttttac tggttgtcgc caactaacta gtccatctcc	GCGCAAAATG	TCGCAATATG AGCGTTATAC	CTGCAATGCT GACGTTACGA	ATTATCGTCA TAATAGCAGT	AGCTTTGGAG TCGAAACCTC	CGCAGGTAGA GCGTCCATCT	101 GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GACGTTACGA AGCGTTATAC CGCGTTTTAC TGGTTGTCGC CAACTAACTA GTCCATCTCC	101
	AGAGTCGAAT TCTCAGCTTA	AAAAAGAAGA TTTTTCTTCT	GAATICAACT ICICCATACT TIGGATAAGG AAATACAGAC ATGAAAAATC TCATIGCTGA GTIGTTATTI AAGCTIGCCC AAAAAGAAGA AGAGTCGAAT CTTAAGITGA AGAGGIATGA AACCIATICC TITAIGICTG TACITITIAG AGIAACGACT CAACAATAAA TICGAACGGG ITTITCIICT ICICAGCITA	GTTGTTATTT CAACAATAAA	TCATTGCTGA AGTAACGACT	ATGAAAATC TACTTTTTAG	AAATACAGAC TTTATGTCTG	TTGGATAAGG	TCTCCATACT AGAGGTATGA	1 GARITUAAUT TUTUCUATAGT TIGGATAAGG AAATACAGAC ATGAAAAATO TCATIGCIGA GTIGTTATIT AAGCITGCCC AAAAAGAA AGAGTUGAAT CTTAAGTIGA AGAGGTAIGA AACCTAITCC TITAIGICIG TACTITITAG AGTAACGACT CAACAATAAA TICGAACGGG TITITUTICT TUTCAGCTIA	7

CAAGACCCTG TGTCCCATGG Trereserre reresarces strengeses GTGTGCCTGC ACAGGGTACC O Ö Ø œ AGACCTAGGC GGACGTTTGG CCTGCAAACC TGCTTCTGTT Ö ſъ Ö AAGAGCGAAG ACCGTGCCGT TGGCACGGCA AATCTGGAAC ſ14 Ω, œ > Ŋ GCTCCGAAAG TACTGATTTA CTTCACCTCC TCTCTCCACT CTGGAGTCCC GCCATCTGAT GAGCAGTTGA GACCTCAGGG ACAGTATAGC TGTCATATCG ഗ > > ტ O ATTACTGTCA GAAGTGGAGG AGAGAGGTGA ഗ AAGCGTTGAA TAATGACAGT Ø × ပ TTCGCAACTT TCATCTTCCC ຜ H ۲ Ø ſυ CGAGGCTTTC ATGACTAAAT GCCAGAAGAC CGGTCTTCTG CCATCTGTCT Δ 臼 CCTAAAGTGA GACTGGTAGT CGTCAGACGT D F I L I I S S L Q GCAGTCTGCA TGTGGCTGCA × 501 ATCAACAGAA ACCAGGAAAA CTGACCATCA TCAAACGAAC TGGTCCTTTT × Ö Д TAGTTGTCTT GGATTTCACT o ø 701

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AGGACAGCAA TCCTGTCGTT S CAGTGTCTCG GTCACAGAGC 囟 ы CCAGGAGAGT GGTCCTCTCA S ω ø GCCCTCCAAT CGGGTAACTC GCCCATTGAG z O CGGGAGGTTA O ü Ø GGTGGATAAC CCACCTATTG z Д TACAGTGGAA ATGTCACCTT × ø CICCGGTTIC GAGGCCAAAG × CTATCCCAGA GATAGGGTCT œ TGAATAACTT ACTTATTGAA z 106

CCCGGACTCG TCACCCATCA AGTGGGTAGT H GCCTGCGAAG CGGACGCTTC ъ > CAAAGICIAC GTTTCAGATG ⊁ > × ACGAGAAACA TGCTCTTTGT X H ы TTTCGTCTGA AAAGCAGACT Ω Ø × CTGCGACTCG GACGCTGAGC GCAGCACCCT ATGTCGGAGT CGTCGTGGGA Y S L S S T L TACAGCCTCA CCTGTCGTGG GGACAGCACC . 🗅 1001

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- GAGCCAACGG CGGCCCGCAA AAATAACAA CGGCTGCGCG TAGAGCTTAC TTGACACACG CGTCCATCTT CGAAACCTCT AATAGCAGTG TTATCGTCAC GCTTTGGAGA ATCTCGAATG AACTGTGTGC GCAGGTAGAA GCCGACGCGC TITITATIGIT CICGGIIGCC 1201
- CATTCCTGAC CCGATGCCAG GAGGTAAAGC GGCGCTGTAC AGGTAGAGGG TTGATTGATC CGCAAAATGA CCAACAGCGG CGCAATATGG SCGTTATACC 1301
 - CCGAGACTTA GCGTTTTACT GGTTGTCGCC AACTAACTAG TCCATCTCCC CCGCGACATG CTCCATTTCG GGCTACGGTC GTAAGGACTG CTGTCATAAA GTTGTCACGG TGAAGCATCC TCGTCAGTAA AAAGTTAATC TTTTCAACAG AAGAAGTTAT CGATTACGTA AGCTGCTGCG 1401
- AGCAGICAIT ITICAAITAG AAAAGIIGIC GACAGIAITI CAACAGIGCC GGCICIGAAI CACGTAAAAA GGGTATCTAG AATTATGAAG AAGAATATCG TACGCAAGTT TCGACGACGC GCTAATGCAT TTCTTCAATA ACTTCGTAGG TTGTAACTAG TTTAATGTAT GTTTTTATT TAGTCGCTTT 1501
- GTAAAGAAGA GTGCATTTT CCCATAGATC TTAATACTTC TTCTTATAGC STII Signal TIR-1 ATCAGGGAAA CAAAAATAAA AAATTACATA AACATTGATC ATGCGTTCAA
- ß GGCCTGGTGC AGCCAGGGGG (CGGACCACG TCGGTCCCCC) CAGACCGCCA GTCTGGCGGT v Ö S AAACGCGTAC GCTGAGGTTC AGCTGGTGGA TTTGCGCATG CGACTCCAAG TCGACCACCT E V Q L V E start heavy chain æ × z A CTATTGCTAC AAGCAAAAA GATAACGATG H ø, TTCGTTTTTT ſz, > TGCATCTATG ACGTAGATAC Σ ഗ ø, 1601 2
- ACCTAATTGT TACCCAACCT AGGGCCTGGA ATGGGTTGGA Ö > TCCCGGACCT ы ტ GCCCCGGGTA CGGGGCCCAT Ö A P ACCAACTATG GTATAAACTG GGTCCGTCAG CATATITGAC CCAGGCAGIC O 24 > N TGGTTGATAC T N Y CTATACCTTC GATATGGAAG Œ, H >+ CAGCTTCTGG (Ö ഗ Þ AACAGGACAC ø TTGTCCTGTG O 1701 43
- ACTIGICGGA TGAACAGCCT ATGGACGTCT TACCTGCAGA o ı X AAGCACAGCA TTCGTGTCGT H S ACACCTCCAA TGTGGAGGTT S H TTTTCTTTAG AGCAAAGTGA AAAAGAAATC Ω ᆸ S [z, TCGTTTCACT E-i 2 TAAAGTTTGC ATTTCAAACG œ 다 자 TATGCTGCGG ATACGACGCC Ω Ø Y A ACTTGGCTGG TGAACCGACC E٠ Ω, ы GGATATGGCC CCTATACCGG Ö 1801 77

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- CCCAGTTCCT Ö TCGACGTCTG AGCTGCAGAC M N GTGACCATAA CACTGGTATT X M H CGCCTTCTCG GCGGAAGAGC S × œ CCGCACTATT ATGTGAACGA TACACTIGCT z > GGCGTGATAA > х н TGCAAAGTAC ACGITICAIG A K AGATAATGAC TCTATTACTG υ **≯** CTGTGACGGC GACACTGCCG > 4 ₽ GCGCGCTGAG CGCGCGACTC Ø 1901 110
- CGGGACCCGA J GGGCACAGCG æ ტ GCACCTCTGG CGTGGAGACC ഗ E TCCTCCAAGA AGGAGGTTCT S × Ŋ TTCCCGGGTA GCCAGAAGGG GGACCGTGGG CCTGGCACCC Д ø CGGTCTTCCC ۷ بو AAGGGCCCAT S Д r CCGGAGGTGG GGCCTCCACC ۲ တ æ CCGICICCIC GGCAGAGGAG ß ß TGGGACCAGT ACCCTGGTCA Н > ᆸ 2001 143
- CCGGCTGTCC IACAGTCCTC GGCCGACAGG CGTGTGGAAG GCACACCITC ĹŁ, ۲ Ξ GGTCGCCGCA CCAGCGGCGT v တ CCGCGGGACT GTGGAACTCA GGCGCCCTGA ы v CACCTIGAGI S z GGGCTTGGCC ACTGCCACAG TGACGGTGTC > ₽ CCCGAACCGG ۵ م ы GGACTACTTC CCTGATGAAG GCCTGGTCAA CGGACCAGTT > ᆈ 2101 177

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- CCGGCTGTCC GGCCGACAGG GCACACCTTC CGTGTGGAAG ſ. H X CCAGCGGCGT GGTCGCCGCA > უ တ GGCGCCCTGA CCGCGGGGACT H Ø ტ GTGGAACTCA GGGCTTGGCC ACTGCCACAG CACCTTGAGT Ø 3 TGACGGTGTC > CCCGAACCGG ш Ω, CCTGATGAAG GGACTACTTC ×
- TGTTCGGGTC Ω, × AACGTGAATC H TTGCACTTAG N V CTACATCTGC GATGTAGACG U **-**>1 CGTGGGTCTG GCACCCAGAC o TCGTCGAACC AGCAGCTTGG S TGTGCCCTCT ACACGGGAGA ഗ U, > CGCACCACTG GCGTGGTGAC > > TCCCTCAGCA AGGGAGTCGT AGGACTCTAC TCCTGAGATG L K
- AAGGAGAAGG TGGCAGTCAG ACCGTCAGTC ഗ AGGACCCCC TCCTGGGGGG ט ы CGTGGACTTG GCACCTGAAC Д TGGCACGGGT ACCGTGCCCA ບ TGTGTACGGG ACACATGCCC CTGTTTTGAG GACAAAACTC × CAAATCTTGT GTTTAGAACA O S AAGTTGAGCC TTCAACTCGG ы CACCTGTTCT GTGGACAAGA Ω
- TCAAGTTGAC CCTGAGGTCA GGACTCCAGT ΞΚ GGTGCTTCTG CCACGAAGAC Ω ω × TGGACGTGAG ACGCACCACC ACCTGCACTC Ω TGCGTGGTGG > > ر د ACTCCAGTGT : TGAGGTCACA GGGCCTGGGG CCCGGACCCC ₽ œ CTCATGATCT GAGTACTAGA ri Z CAAGGACACC GTTCCTGTGG Ω GGGGTTTTGG CCCCAAAACC Δ,
- GCAGGACGTG x GCGTCCTCAC CGCAGGAGTG CGTGTGGTCA GCACACCAGT > GTCGTGCATG S T Y 1 CAGCACGTAC AGCAGTACAA TCGTCATGTT z X GGCGCCCTCC CCGCGGGAGG [1] æ Д CAAGACAAAG GTTCTGTTTC F X × TGCATAATGC ACGIATIACG K Z = CCGCACCTCC GGCGTGGAGG ы ک ق GTACGTGGAC CATGCACCTG 2501
- CCCGTCGGGG а, О CAAAGCCAAA GTTTCGGTTT A × AAACCATCTC TTTGGTAGAG CCCATCGAGA GGGTAGCTCT CCTCCCAGCC GGAGGGTCGG ۵ م CCAACAAAGC GGTTGTTTCG ø × z TGCAAGGTCT ACGITCCAGA × GGAGTACAAG CCTCATGTTC × ы TGAATGGCAA ACTIACCGIT Ö Z CAGGACTGGC GTCCTGACCG 2601 343
- GGTCGCTGTA GGCTTCTATC CCGAAGATAG CCTGGTCAAA GGACCAGTIT GCCTGACCTG CGGACTGGAC TTGGTCCAGT AACCAGGTCA o GATGACCAAG CTACTGGTTC × E Σ CCCGGGAAGA GGCCCTTCT Œ æ CIGCCCCCAT GACGGGGGTA Д GGTGTACACC CCACATGTGG H ۲ ۸ GAGAACCACA CTCTTGGTGT 2701 377
- GTCGTTCGAG TCTTCCTCTA AGAAGGAGAT CTGCCGAGGA D G S F GACGGCTCCT GCTGGACTCC CGACCTGAGG ഗ ᆸ CGCCTCCCGT GCGGAGGGCA Д, Д TACAAGACCA ATGTTCTGGT E٠ × GGAGAACAAC CCICITGILG z Ή TACCCGTCGG ATGGGCAGCC o TGGGAGAGCA ACCCTCTCGT GCGCCACCTC CGCCGTGGAG 2801 410
- GAGAGGGACA GCAGAAGAGC CGTCTTCTCG o ACCACTACAC TGGTGATGTG GCTCTGCACA CGAGACGTGT H A GATGCATGAG CTACGTACTC G3 **::** Σ GTACGAGGCA CATGCTCCGT > S O TTGCAGAAGA AACGICITCI Ĺż, GCAGCAGGGG CGTCGTCCCC œ o AGAGCAGGTG TCTCGTCCAC œ ACCGTGGACA TGGCACCTGT T V D 2901
- TATCATCGAT AAACTGTCGA ATAGTAGCTA TTTGACAGCT TTAACTCATG AATTGAGTAC AAAAAATAAC TTTTTTTG CIGCCGGGAT CICAGGGATT GCGAGCCAAC GGCGGCCCGC 5055500500 CGCTCGGTTG GAGTCCCTAA GACGCCCTA ATAAGCATGC TATTCGTACG CTCCGGGTAA GAGGCCCATT

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GGGACCTACG ACATCCGTAT CCGAACCAAT ACGGCCATGA CGGCCCGGAG AACGC TGCCGGTACT TGTAGGCATA GGCTTGGTTA CCCTGGATGC 3201

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GGP 4	TTA TTA	GGA	ACC AATO	TCG AGC	CTG GAC	090 ∢		GTGP CACT	AGA TCT
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GIGCACCAAT GCITCTGGCG TCAGGCAGCC CACGIGGITA CGAAGACCGC AGICCGICGG	CGTTCTGGAT AATGTTTTTT GCAAGACCTA TTACAAAAA	AATTGTGAGC GGATAACAAT TAAGCTTAGG TTAACACTCG CCTATTGTTA ATTCGAATCC	GCATO CGTAO	CAGCTTATGC ACTGGGTGCC TCGCTGGGTC GTCGAATACG TGACCCACGG AGCGACCCAG A Y A L G A S L G R	GATGCATITG CTGATAAGAG CTACGTAAAC GACTATICIC D A F A D K S	GCGAAGATGG AAAAAGACGC GGCTGATAAC CGCTTCTACC TTTTTCTGCG CCGACTATTG A K M E K D A A D N	GGTAGTAGAA CCATCATCTT V V E	CGACAACTCT TACACCCGTG GTGAACCGCT TTCTTTCCGT GCTGTTGAGA ATGTGGGCAC CACTTGGCGA AAGAAGGCA D N S Y T R G B P L S F R	TATT ATAA(I
	TCC C	TGG A	366 A	TGC A		TGG P		SAGA A	TGG T
GACG.	GCAC	TGTG	GCCGTTGC CGGCAACG A V Ä	CTTA:	TGTT ACAP V	BAAGAT TTCTA K M	GCAAATI V Y.	CGACAACTCT GCTGTTGAGA D N S	ATCAAACTGG TAGTTTGACC I K L V
r can	A. 660	TA A	# 600 \$ 000 \$	T CAGC		000 A	766 700 A	r cgac a gcrc	A ATC
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GIGICATGGI CGGIGAICGC CAGGGIGCCG ACGCGCAICT CGACIGCACG CACAGIACCA GCCACIAGCG GICCCACGGC IGCGCGIAGA GCIGACGIGC	TGTCGCTCAA GGCGCACTCC ACAGCGAGTT CCGCGTGAGG	TTCTGAAATG AGCTGTTGAC AATTAATCAT CGAACTAGTT TAATGTGTGG AATTGTGAGC GGATAACAAT TAAGCTTAGG AAGACTTTAC TCGACAACTG TTAATTAGTA GCTTGATCAA ATTACACACC TTAACACTCG CCTATTGTTA ATTCGAATCC	GACCACAATG GCCGTTGCCC TGCATGCACC AATCACTTTT GCTGCTGAAG CTGGTGTTAC CGGCAACGGG ACGTACGTGG TTAGTGAAAA CGACGACTTC T T M A V A L H A P I T F A A E A	CAAAAATGAC GATCAGAAAT CAGCTTATGC ACTGGGTGCC TCGCTGGGTCGTTTTACTG CTAGTCTTTA GTCGAATACG TGACCCACGG AGCGACCCAG K N D D Q K S A Y A L G A S L G R	GATAAAGATC AGCTGATCGC CTATTTCTAG TCGACTAGCG D K D Q L I A	TTCTGCTCAG GCGAAGATGG AAAAAGACGC AAGACGAGTC CGCTTCTACC TTTTTCTGCG S A Q A K M E K D A	TITGCCAAAG AGAAAGGIGI GAAAACCICT TCAACIGGIC IGGITIAICA AAACGGITIC ICITICCACA CITIIGGAGA AGTIGACCAG ACCAAAIAGI F A K E K G V K I S S I G L V Y Q	CAAAGGTACG CTGATCGACG GTAAAGAGTT GTTTCCATGC GACTAGCTGC CATTTCTCAA K G T L I D G K E F	GGTCTGAAGA ACATCAAGAA AGGCGGTAAG ATCAAACTGG TTATTCCACC AGAACTGGCT TACGGCAAAG CCAGACTTCT TGTAGTTCTT TCCGCCATTC TAGTTTGACC AATAAGGTGG TCTTGACCGA ATGCCGTTTC G L K N I K K G G K I K L V I P P E L A Y G K A
ည္မွင္တင္မ	TCG	CAT		IGAC ACTG D	AGATC CCTAG D Q		TCT BAGA S	CGACG CTGC D G	GAA
GGGTG	ATAAT TATT	TTAAT	CGCTGCTGGC GCGACGACGG L L A	CAAAATGAC GTTTTACTG K N D	TAAAG ATTTC K	GCGTGAAGTC CGCACTTCAG V K S	AAACC TTTGC T	CTGATCC GACTAGC L I I	CATCAAGA STAGTTCT: I K K
ဂ် ရှိ ရှိ	F 6	A P	ម្ម ស្ត្រ	F G GT ×		ပ္စ္ ပိုစ္ပဲ ပိုစ္စဲ		o o G C	AHN
BATCG TAGC	VTCAC PAGTG	STTGA SAACT	AGTAA TCATT V T	AGCGT.	aaact ittga k l	AGCT TCGA A	AGGTGT CCACA G V	AGGTAC CCCATG G T	rctgaaga agacttct L K N
GIGICAIGGI CGGIGAICGC CACAGIACCA GCCACIAGCG	TGTGCAGGTC GTAAATCACT GCATAATTCG ACACGTCCAG CATTTAGTGA CGTATTAAGC	AGCTO	GAAATCACTG TTTAAAGTAA CTTTAGTGAC AAATTTCATT KSLFKVT PASLART	GCTGACAGCA AAGCAGCGTT CGACTGTCGT TTCGTCGCAA A D S K A A F	CATCAAACTG GTAGTTTGAC I K L	TCTACAAGCA TTCGAAGCTC GCGTGAAGTC AGATGTTCGT AAGCTTCGAG CGCACTTCAG L Q A F E A R V K S	TTTGCCAAAG AGAAAGGTGT AAACGGTTTC TCTTTCCACA F A K E K G V	CAAAGGTACG GTTTCCATGC K G T	GGTCTGAAGA ACATCAAGAA CCAGACTTCT TGTAGTTCTT G L K N I K K
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GTCAT	TGCAC	CTGAZ	AT GAAATCACT TA CTTTAGTG/ M K S L ^fkpA start	TGACA ACTG1 D &	AAAAACTGGG TTTTTGACCC K L G	TCTACAAGCA AGATGTTCGT L Q A	TGCCI ACGGI	AGTGAA TCACTT	GAC!
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rgctgtg Acgacac	ratgg vtacc	TARAC	TTTA RAAT	ACAGO FGTCG	VACAA FTGTT	ACAGA(NGTCTC Q T	GAGAA CTCTT E K	ACTGTTG FGACAAC F V V	5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5 5
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Arcgargaar reargered rageractra agracgaeae elai	ATCGGAAGCT GIGGIAIGGC IGIGCAGGIC GIAAAICACT GCAIAATICG IGICGCICAA GGCGCACTCC IAGCCIICGA CACCAIACCG ACACGICCAG CAITIAGIGA CGIAITIAAGC ACAGCGAGII CCGCGIGAGG	CATAACGGTT CTGGCAAATA GTATTGCCAA GACCGTTTAT	301 ATTCTAGAGG GAAGATTTAT GAAATCACTG TTTAAAGTAA CGCTGCTGGC TAAGATCTCC CTTCTAAATA CTTTAGTGAC AAATTTCATT GCGACGACCG N K S L F K V T L L A Å ÉKpå start	CTGCAAAACC TGCTACAGCT GCTGACAGCA.AAGCAGCGTT GACGTTTTGG ACGATGTCGA CGACTGTCGT TTCGTCGCAA A K P A T A A D S K A A F	rcta AGAT L	GACCAAGAGA TCGAACAGAC CTGGTTCTCT AGCTTGTCTG D Q E I E Q T	GTAAAGAGTA CCGCGAGAAA CATTTCTCAT GGCGCTCTTT K E Y R E K	GAAAGACAGC GATACTGTTG TAGTGAACTA CTTTCTGTCG CTATGACAAC ATCACTTGAT K D S D T V V V N Y	CTGGACGGTG TTATCCCGGG GACCTGCCAC AATAGGGCCC L D G V I P G
ATCGATC TAGCTAC	CGGA	TAAC(ATTG(TCTA(AGAT(GCAAA CGTTT A K	ACTCT TGAGI	CCAAC GGTTC Q E	AAAGI TTTCI K E	AAGAC TTCTC D	CTGGACC GACCTGC L D C
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METHODS AND COMPOSITIONS FOR INCREASING ANTIBODY PRODUCTION Reilly et al. Attorney Docket P1957R1 Sheet 15 of 33

1001 CGGGTGTTCC GGGGATCCCA CCGAATTCTA CCCTGGTGTT TGACGTAGAG CTGCTGGATG TGAAACCAGC GCCGAAGGCT GATGCAAAGC CGGAAGCTGA GCCCACAAAGG CCCCTAGGGT GGCTTAAGAT GGGACCACAA ACTGCATCTC GACGACCTAC ACTTTGGTCG CGGCTTCCGA CTACGTTTCG GCCTTCGACT	G I P PNST LVF DVE LLD V KPA PKA DAKP EAD				
TGAAACCAGC GCC ACTTTGGTCG CGG	K P A				
CTGCTGGATG	V. O 1 1				
TGACGTAGAG	ы >				
CCCTGGTGTT	F. C.	AAAGCTAGC	TTTCGATCG		ANDOT
CCGAATTCTA GGCTTAAGAT	S N	СТАААААТА	GATTTTTAT	D S A K K O	
GGGGATCCCA	о Н	GCAGATTCTG	ACCCTTTCGG CGTCTAAGAC GATTTTTTAT TTTCGATCG	ADSA	
CGGGTGTTCC	229 G V P	1101 TGCGAAAGCC GCAGATTCTG CTAAAAATA AAAGCTAGC	ACGCTTTCGG	262 A K A	
1001	229	1101		262	

FIG. 5B

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TCGA	AGCT	
AGAG	5 5	
SAAGA	CTTCT	
AAAAA	TTTT	
2000	10000	
GAATTCAACT TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAATC TCATTGCTGA GTTGTTATTT AAGCTTGCCC AAAAAGAAGA AGAGTCGAAT	CITAAGITGA AGAGGIAIGA AACCIAITCC ITIAIGICIG IACITITIAG AGIAACGACT CAACAAIAAA IICGAACGGG IITITCTICI ICICAGCITA	
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3A GT	5 5	
TGCT	ACGA	
TCAT	AGTA	
AAATC	TTTAG	
ATGAA	TACTT	
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AGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG	ICCATCT ICGAAACCIC TAATAGCAGI GACGITACGA AGCGITATAC CGCGITITIAC IGGIIGICGC CAACIAACIA GICCAICICC
GTTGATTGAT	CAACTAACTA
GGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAG	TGGTTGTCGC
GCGCAAAATG	CGCGTTTTAC
TCGCAATATG	AGCGTTATAC
CTGCAATGCT	GACGTTACGA
ATTATCGTCA	TAATAGCAGT
AGCTTTGGAG	TCGAAACCTC
CGCAGGTAGA	GCGTCCATCT
101 GAACTGTGTG CGCA	CTTGACACAC GCGT
101	

²⁰¹ GGGCGCTGTA CGAGGTAAAG CCCGATGCCA GCATTCCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTCAGTA CCCGCGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA ITTCTTCAAT AACTTCGTAG GAGCAGTCAT

⁴⁰¹ TCACGTAAAA AGGGTATCTA GAATTATGAA AAAGAATATC GCATTTCTTC TTGCATCTAT GTTCGTTTTT TCTATTGCTA CAAACGCGTA CGCTGATATC AGTGCATTTT TCCCATAGAT CTTAATACTT TTTCTTATAG CGTAAAGAAG AACGTAGATA CAAGCAAAAA AGATAACGAT GTTTGCGCAT GCGACTATAG 1 S I A T N A Y A D I anti-TF 11ght chain^ M K K N I A F L L A start STII signal TIR 7

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TCCCCGAG CTCCCTGTCC GCCTCTGTGG GCGATAGGGT CACCATCACC TGCAGAGCCA GTCGCGACAT CAAGAGCTAT CTGAACT	NGGGGCTC GAGGGACAGG CGGAGACACC CGCTATCCCA GTGGTAGTGG ACGTCTCGGT CAGCGCTGTA GTTCTCGATA GACTTGACC;	V G D R V T I T C
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AAG TACTGATITA CTATGCTACT AGTCTCGCTG AAGGAGTCCC TTCTCGCTTC TCTGGATCCG GTTCTGGGAC	FICCTITI CGAGGCTTIC ATGACTAAAI GATACGATGA TCAGAGCGAC TICCTCAGGG AAGAGCGAAG AGACCTAGGC CAAGACCCTG	IY Y.AT SLAE GVP SRF SGSG SGT
AAGGAGTCCC 1	TTCCTCAGGG 1	<u>а</u> У
AGTCTCGCTG 1	TCAGAGCGAC 1	SLAB
CTATGCTACT .	GATACGATGA	YAT
TACTGATTTA	ATGACTAAAT	LI
A GCTCCGAAAG	CGAGGCTTTC	GKAPKV LI
AGGAAA		P G K
601 ATCAACAGAA ACC	TAGTTGTCTT TG	20 Q Q
9		•

TGACCATCA GCAGTCTGCA GCCAGAAGAC TTCGCAACTT ATTACTGTCT TCAGCACGGA GAGTCTCCAT GGACATTTGG ACAGGGTACC	SACTGGTAGT CGTCAGACGT CGGTCTTCTG AAGCGTTGAA TAATGACAGA AGTCGTGCCT CTCAGAGGTA CCTGTAAACC TGTCCCATGG	TIS SLO PED FATY YCL OHG ESPW TFG OGT
TCAGCACGGA GA	AGTCGTGCCT CT	D H C
ATTACTGTCT	TAATGACAGA	Y C F
TTCGCAACTT	AAGCGTTGAA	FATY
GCCAGAAGAC	CGGTCTTCTG	ы Б Б
GCAGTCTGCA	CGTCAGACGT	S 1 0
CTGACCATCA	GACTGGTAGT	LTIS
. GGATTACACT	CCTAATGTGA	D Y T
701		93

⁸⁰¹ AAGGTGAGA TCAAACGAAC TGTGGCTGCA CCATCTGTCT TCATCTTCCC GCCATCTGAT GAGCAGTTGA AATCTGGAAC TGCTTCTGTT GTGTGCCTGC CACACGGACG ACGAAGACAA TTAGACCTTG Ö ഗ ACACCGACGT GGTAGACAGA AGTAGAAGGG CGGTAGACTA CTCGTCAACT TICCACCICT AGIIIGCIIG œ × ж ч 126

CTITICAACA GCIGICATAA AGTIGICACG GCCGAGACIT ATAGICGCIT IGITITIAIT TITIAAIGIA ITIGIAACIA GIACGCAAGI TITICAATTA GAAAAGITGI CGACAGIATI TCAACAGIGC CGGCICTGAA IAICAGCGAA ACAAAAATAA AAAATTACAI AAACATIGAI CAIGCGITCA AAAAGTTAAT 301

GTCACAGAGC AGGACAGCAA CAGTGTCTCG TCCTGTCGTT Œ CTCCGGTTTC ATGTCACCTT CCACCTATTG CGGGAGGTTA GCCCATTGAG GGTCCTCTCA E A K V Q W K V D N A L Q S G N S Q E S GAGGCCAAAG TACAGTGGAA GGTGGATAAC GCCCTCCAAT CGGGTAACTC CCAGGAGAGT CTATCCCAGA GATAGGGTCT ĸ ч Б ACTTATTGAA 901 TGAATAACTT z z

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1001 GGACAGCACC TACAGCCTCA GCAGCACCCT GACGCTGAGC AAAGCAGACT ACGAGAAACA CCTGTCGTGG ATGTCGGAGT CGTCGTGGGA CTGCGACTCG TTTCGTCTGA TGCTCTTTGT 193 D S T Y S L S S T L T L S K A D Y E K H	GGACAGCACC TACAGCCTCA CCTGTCGTGG ATGTCGCAGT D S T Y S L S	GCAGCACCCT CGTCGTGGGA S T L	GACGCTGAGC CTGCGACTCG T L S	AAAGCAGACT TTTCGTCTGA K A D Y		CAAAGTCTAC GCCTGCGAAG TCACCCATCA GTTTCAGATG CGGACGCTTC AGTGGGTAGT K V Y A C E V T H Q	GCCTGCGAAG CGGACGCTTC A C E V	GCCTGCGAAG TCACCCATCA CGGACGCTTC AGTGGGTAGT A C E V T H Q	GGGCCTGAGC CCCGGACTCG G L S
TCGCCCGTCA AGCGGGCAGT	CAAAGAGC GTTTCTCG	CAACAGO		GAGTGTTAAT TAAATCCTCT CTCACAATTA ATTTAGGAGA	GAGTGTTAAT TAAATCCTCT ACGCCGGACG CTCACAATTA ATTTAGGAGA TGCGGCCTGC	ACGCCGGACG CATCGTGGCG AGCTCGGTAC CCGGGGGATCT TGCGGCCTGC GTAGCACCGC TCGAGCCATG GGCCCCTAGA	AGCTCGGTAC TCGAGCCATG	CCGGGGGATCT	AGGCCTAACG TCCGGATTGC
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1201 CTCGGTTGCC GAGCCAACGG	CTCGGTTGCC GCCGGGCGTT GAGCCAACGG CGGCCCGCAA	TTTTATTGTT AAAATAACAA	GCCGACGCGC ATCTCGACTG CGGCTGCGCG TAGAGCTGAC	ATCTCGACTG TAGAGCTGAC		CAATGCTTCT GTTACGAAGA	GGCGTCAGGC CCGCAGTCCG	GGCGTCAGGC AGCCATCGGA CCGCAGTCCG TCGGTAGCCT	AGCTGTGGTA TCGACACCAT
1301 TGGCTGTGCA ACCGACACGT	TGGCTGTGCA GGTCGTAAAT CACTGCATAA TTCGTGTCGC TCAAGGCGCA ACCGACACGT CCAGCATTTA GTGACGTATT AAGCACAGCG AGTTCCGCGT	CACTGCATAA	TTCGTGTCGC	TCAAGGCGCA AGTTCCGCGT	TTCGTGTCGC TCAAGGCGCA CTCCCGTTCT GGATAATGTT TTTTGCGCCG ACATCATAAC AAGCACAGCG AGTTCCGCGT GAGGGCAAGA CCTATTACAA AAAACGCGGC TGTAGTATTG	GGATAATGTT CCTATTACAA	TTTTGCGCCG AAAACGCGGC	ACATCATAAC TGTAGTATTG	GGTTCTGGCA CCAAGACCGT
1401 AATATTCTGA TTATAAGACT 1	AATATTCTGA AATGAGCTGT TGACAATTAA TCATCGAACT AGTTTAATGT TTATAAGACT TTACTCGACA ACTGTTAATT AGTAGCTTGA TCAAATTACA	tgacaattaa actgitaatt	TCATCGAACT AGTTTAATGT AGTAGCTTGA TCAAATTACA	AGTTTAATGT TCAAATTACA	GTGGAATTGT CACCTTAACA		CAATTAAGCT GTTAATTCGA Start ST	CAATTAAGCT TAGGATCTAG GTTAATTCGA ATCCTAGATC Start STII signal I	3 AATTATGAAG 3 TTAATACTTC M K TIR 3^
1 AAGAATATTG TTCTTATAAC 3 K N I A	1501 AAGAATATTG CGTTCCTACT TTCTTATAAC GCAAGGATGA 3 K N I A F L L	TGCCTCTATG ACGGAGATAC ASM	TTTGTCTTTT AAACAGAAAA F V F S	CTATAGCTAC GATATCGATG I A T		GCT	GAGGTTC AGCTGGTGGA G CTCCAAG TCGACCACCT C E V Q L V E · · · · · · · · · · · · · · · · · ·	GTCTGGCGGT CAGACCGCCA S G G	GGCCTGGTGC CCGGACCACG G L V Q
1601 AGCCAGGGGG TCGGTCCCCC	AGCCAGGGGG CTCACTCCGT TCGGTCCCCC GAGTGAGGCA P G G S L R	TTGTCCTGTG AACAGGACAC L S C A	CAGCTTCTGG GTCGAAGACC A S G	CTTCAATATT GAAGTTATAÄ F N I		ACATGCACTG TGTACGTGAC M H W	GGTCCGTCAG CCAGGCAGTC V R Q	GCCCCGGGTA CGGGGCCCAT A P G K	AGGCCTGGA TCCCGGACCT G L E
01 ATGGGTTGGA TACCCAACCT 70 W V G	1701 AIGGGITGGA ITGAITGAIC CAGAGCAAGG TACCCAACCI AACTAACTAG GICTCGITCC 70 W V G L I D P E Q G	CAGAGCAAGG GTCTCGTTCC E Q G		TATGACCCGA ATACTGGGCT Y D P K		CCGTGCCACT ATAAGCGCTG ACAATTCCAA GGCACGGTGA TATTCGCGAC TGTTAAGGTT R A T I S A D N S K	ATAAGCGCTG TATTCGCGAC I S A D	ACAATTCCAA TGTTAAGGTT N S K	AAACACAGCA TTTGTGTCGT N T A
1801 TACCTGCAGA ATGGACGTCT 103 Y L Q M	TACCTGCAGA TGAACAGCCT ATGGACGTCT ACTTGTCGGA Y L Q M N S L	GCGTGCTGAG CGCACGACTC R A E	GACACTGCCG CTGTGACGGC D T A V	TCTATTATTG AGATAATAAC Y Y C	TGCTCGAGAC ACGAGCTCTG A R D	ACGGCCGCTT ACTTCGACTA TGCCGGCGAA TGAAGCTGAT T A A Y F D Y	ACTTCGACTA TGAAGCTGAT F D Y	CTGGGGTCAA GACCCCAGTT W G Q	GGAACCCTGG CCTTGGGACC G T L V
1901 TCACCGTCTC AGTGGCAGAG 137 T V S	TCACCGTCTC CTCGGCCTCC AGTGGCAGAG GAGCCGGAGG T V S S A S	ACCAAGGGCC TGGTTCCCGG T K G P T AApaI	CATCGGTCTT GTAGCCAGAA S V F	CCCCCTGGCA GGGGGACCGT P L A		CCCTCCTCCA AGAGCACCTC GGGAGGAGGT TCTCGTGGAG P S K S T S	TGGGGGCACA ACCCCCGTGT G G T	GCGGCCCTGG CGCCGGGACC A A L G	GCTGCCTGGT CGACGGACCA C L V
2001 CAAGGACTAC GTTCCTGATG 170 K D Y	CAAGGACTAC TTCCCCGAAC GTTCCTGATG AAGGGGCTTG K D Y F P E P	CGGTGACGGT GCCACTGCCA V T V	GTCGTGGAAC CAGCACCTTG S W N	TCAGGCGCCC AGTCCGCGGG S G A L	TGACCAGCGG ACTGGTCGCC T S G	CGTGCACCC GCACGTGTGG V H T	TTCCCGGCTG AAGGGCCGAC F P A V	TCCTACAGTC AGGATGTCAG L Q S	CTCAGGACTC GAGTCCTGAG S G L

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TGTCTCCGGG AACAATTGAG TACAAACTGT CGAATAGTAG CTATTCGAAA CATCGCCGTG CTCACCGTGG GAGTGGCACC ACAGAGGCCC AGGGGGGTTT TTCCACCTGI > Δ o ۲ н CTACAGCAAG AGCCTCTCCC TCGGAGAGGG GCTTATCATC GICTICCICI CAGAAGGAGA CACCGTCCTG GTGGCAGGAC AAAGGGCAGC TTTCCCGTCG ATCCCAGCGA CAGCAACACC GTCGTTGTGG TCAAGTTCAA AGTTCAAGTT S ы Ö ഗ ഗ × CCTTCTTCCT CACGCAGAAG TIGITAACIC AIGITIGACA CTGGGACTCC TCAGCGTCCT ATGGCACACC AGTCGCAGGA CTCCAAAGCC AAAGGCTTCT TTTCCGAAGA GGAAGAAGGA GTGCGTCTTC CCCTGGCAGT GACCCTGAGG GAGGTTTCGG ATCACAAGCC GGGACCGTCA TAGTGTTCGG Ø × o × U Ħ Ö Д AGGCTGCCGA AGAAAACCAT GACGGACCAG TGTTGGTGAT TGCAACGTGA CTCGGTGCTT TACCGTGTGG TCTTTTGGTA ACAACCACTA AACTCCTGGG TTGAGGACCC CTGCCTGGTC TCCGACGGCT ACGTTGCACT GAGCCACGAA > ı ы ы ı œ z z ы ß CTCCGAGACG TGCGACGGCC CTAGAGTCCC TAACGCTCGG TTGCCGCCGG GCGTTTTTTA ACGCTGCCGG GATCTCAGGG ATTGCGAGCC AACGGCGGCC CGCAAAAAT GACCTACATC GTTGTCGTGC GGTCGTGGAC CAACAGCACG GCCCCCATCG CGGGGGTAGC TCAGCCTGAC AGTCGGACTG CGTGCTGGAC GCACGACCTG GAGGCTCTGC TGGTGGACGT ACCACCTGCA CTGGATGTAG CCAGCACCTG H Ω Д Ω ഗ × Ω, 4 > ۲ z A Ω, TICITGGICC GCACTACGTA TGGGCACCCA GGGTGGCACG TGTACGCACC > AGGAGCAGTA AAGAACCAGG CCACGCCTCC GGTGCGGAGG CGTGATGCAT ACATGCGTGG AGCCCTCCCA TCGGGAGGGT CCCACCGTGC TCCTCGTCAT ACCCGTGGGT ı ت م ρ. o > Д o ۲ ы Σ ပ z Ö ы > 4 Д CTCACACATG AGAGATGACC TCTCTACTGG CCCTTGCAGA AGAGTACGAG G N V F S C S TCTAGCAGCT AGATCGTCGA AAGCCGCGGG (11) AACTACAAGA TTGATGTTCT TCTCATGCTC ы GAGTGTGTAC CCCTGAGGTC GGGACTCCAG Tragadacc TCTCCAACAA AGAGGTTGTT H > ഗ × œ z H Σ 田 N ρ, ល Д × GACTGTGCCC CTGACACGGG TGCCAAGACA AAGTGCAAGG > CATCCCGGGA CGGCCTCTTG TGTGACAAAA ACACTGTTTT TCTCCCGGAC AGAGGGCCTG ACGGTTCTGT TTCACGTTCC GTAGGGCCCT GCCGGAGAAC GGGAACGTCT Z υ × O D R ĸ p4 Ħ > × တ ഗ H 4 Д GTGGCAGCAG CACCGTCGTC CGGGTTTAGA TGGGAGTACT AGGTGCATAA TCCACGTATT CAAGGAGTAC GITCCICAIG ACCCTGCCCC TGGGACGGGG GCAATGGGCA CGTTACCCGT GCAGCGTGGT CGTCGCACCA GCCCAAATCT ACCCTCATGA K O > ø S r Z Д Ö × M O ഗ z H ATTTATTCGT GAGTGGGAGA ACAAGAGCAG TAAATAAGCA GACGGCGTGG CTGCCGCACC ω ACAGGTGTAC TGTTCTCGTC ATGAGGGAGT TGGGTTCCTG GGCTGAATGG TGTCCACATG CTCACCCTCT AGAAAGTTGA TCTTTCAACT ACCCAAGGAC Ω × > 囟 r z > ᅜ **Σ** ω s ¥ Ö × × o × 2701 2801 2201 237 2301 2401 2501 403 437

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CAAGACCCTG AGACCTAGGC (S G S G TCTGGATCCG AAGAGCGAAG TTCTCGCTTC [z, TTCCTCAGGG AAGGAGTCCC ۵ م Ö TCAGAGCGAC I AGTCTCGCTG GATACGATGA CTATGCTACT ø CGAGGCTTTC ATGACTAAAT TACTGATTTA GCTCCGAAAG A P K ACCAGGAAAA TGGTCCTTTT v ATCAACAGAA TAGTTGTCTT 601 9

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H CGGACGCTTC GCCTGCGAAG ы υ CAAAGTCTAC GTTTCAGATG ACGAGAAACA TGCTCTTTGT × ы TTTCGTCTGA AAAGCAGACT Ω X A GACGCTGAGC CTGCGACTCG E GCAGCACCCT CGTCGTGGGA E TACAGCCTCA ATGTCGGAGT S GGACAGCACC CCTGTCGTGG 1001 193

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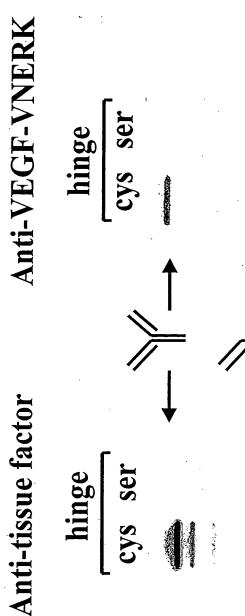
WETHODS AND COMPOSITIONS FOR INCREASING ANTIBODY PRODUCTION Reilly et al. Attorney Docket P1957R1 Sheet 22 of 33

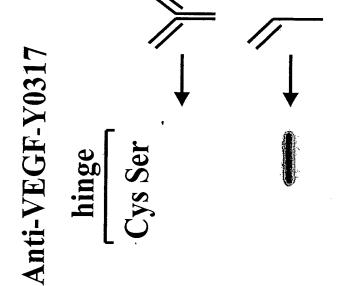
Anti-VEGF VNER

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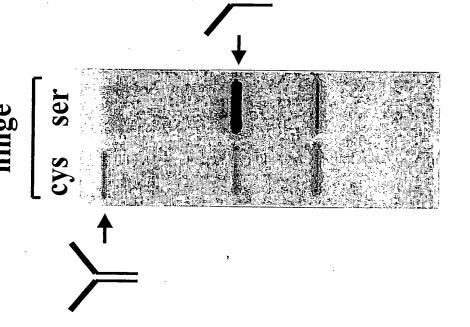
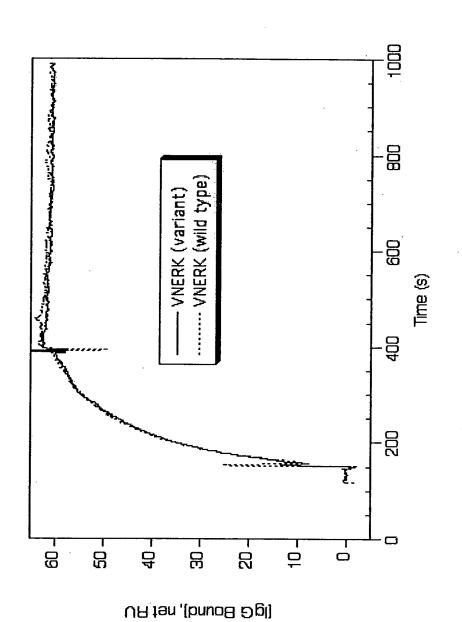
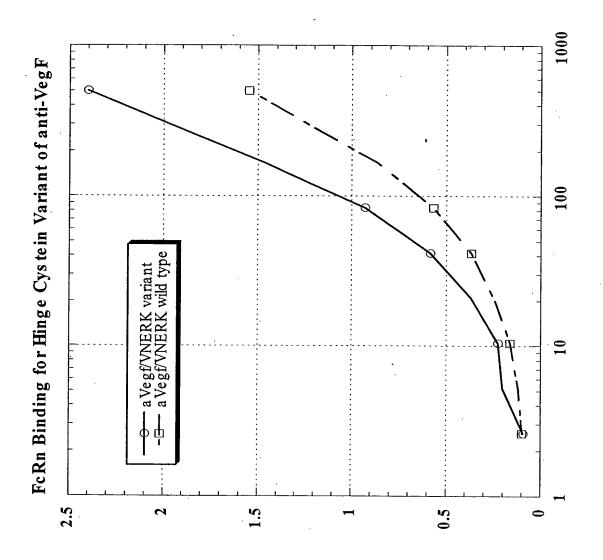


FIG. 11





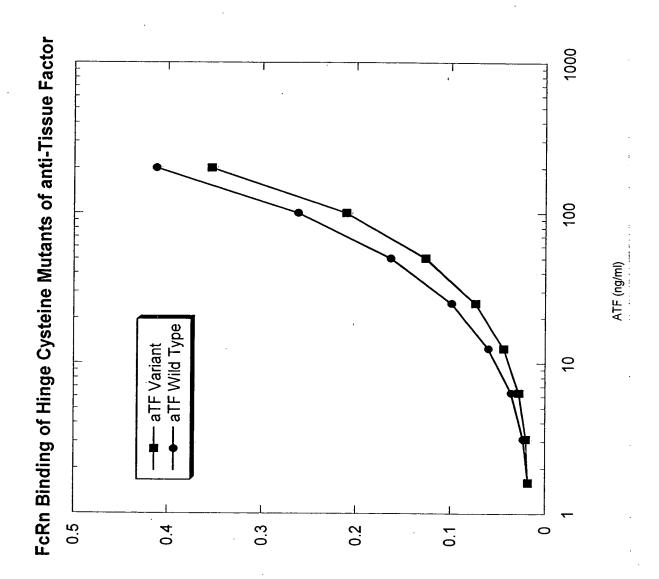




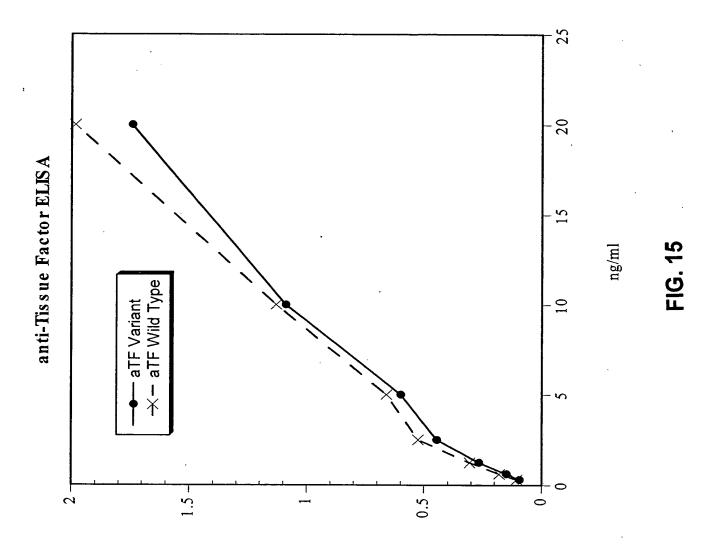
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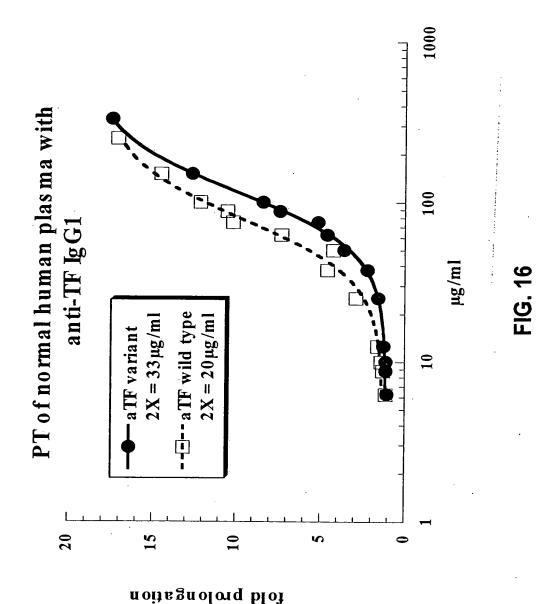


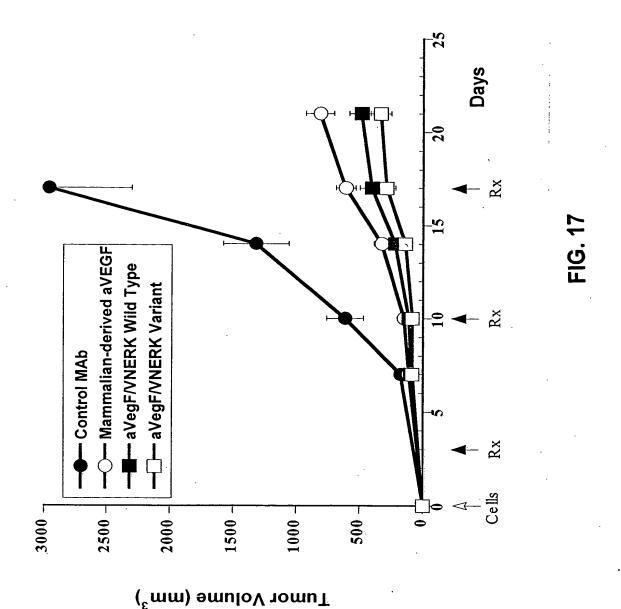


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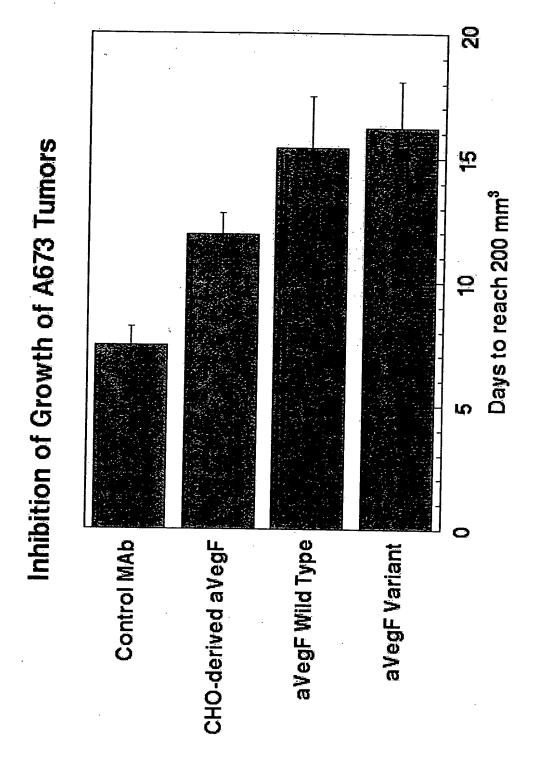


FIG. 1

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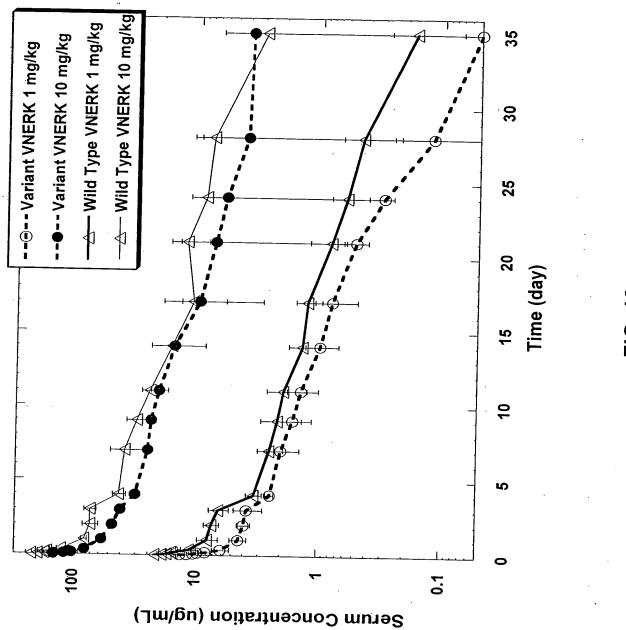


FIG. 15